SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Endovascular Graft

Device Trade Name: Valiant Navion™ Thoracic Stent Graft System

Device Procode: MIH

Applicant's Name and Address: Medtronic Vascular
3676 Unocal Place
Santa Rosa, CA 95403
USA

Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P100040/S036

Date of FDA Notice of Approval: October 19, 2018

The Valiant Navion™ Thoracic Stent Graft System is Medtronic Vascular's next generation thoracic stent graft system, based on the Valiant® Thoracic Stent Graft with the Captivia® Delivery System.

The original PMA (P100040) for the Valiant® Thoracic Stent Graft with the Captivia® Delivery System was approved on April 1, 2011 for the endovascular repair of fusiform aneurysms and saccular aneurysms/penetrating ulcers of the descending thoracic aorta (DTA). The indications for use were expanded to include the treatment of isolated lesions (excluding dissections) of the DTA in patients who have appropriate anatomy via P100040/S008 on October 26, 2012, based on the submission of data for the treatment of traumatic transections. The indications for use were further expanded for the Valiant® Thoracic Stent Graft with the Captivia® Delivery System via P100040/S012 on January 22, 2014 to include the treatment of all lesions of the DTA, including Type B dissections. The Summaries of Safety and Effectiveness Data (SSED) to support the original approval and the expanded indications are available on the CDRH website and are incorporated by reference here.

Original PMA Approval:
https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100040B.pdf

Indication Expansion (P100040/S008):
https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100040S008B.pdf

Indication Expansion (P100040/S012):
https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100040S012B.pdf

This panel-track PMA Supplementwas submitted to obtain approval of the Valiant Navion™ Thoracic Stent Graft System, a modified device design from the Valiant® Thoracic Stent Graft with the Captivia® Delivery System, for the treatment of all lesions of the DTA including, but not limited to, aneurysm, Type B dissections, and transections.

II. INDICATIONS FOR USE

The Valiant Navion™ Thoracic Stent Graft System is indicated for the endovascular repair of all lesions of the descending thoracic aorta (DTA) in patients having the appropriate anatomy including:

- iliac or femoral artery access vessel morphology that is compatible with vascular access techniques, devices, or accessories;
- nonaneurysmal aortic diameter in the range of:
  - 16 mm to 42 mm for fusiform and saccular aneurysms/penetrating ulcers
  - 16 mm to 44 mm for blunt traumatic aortic injuries
  - 19 mm to 45 mm for dissections;
- proximal landing zone (nonaneurysmal aortic proximal neck length for fusiform and saccular aneurysms/penetrating ulcers *or* nondissected length of aorta proximal to the primary tear for blunt traumatic aortic injuries and dissections) of:
  - ≥ 20mm for FreeFlo configuration
  - ≥ 25mm for CoveredSeal configuration; and
- nonaneurysmal aortic distal neck length ≥ 20mm for FreeFlo and CoveredSeal configurations for fusiform and saccular aneurysms/penetrating ulcers.

III. CONTRAINDICATIONS

The Valiant Navion™ Thoracic Stent Graft System is contraindicated in the following patient populations:

- Patients who have a condition that threatens to infect the graft
- Patients who are sensitive to or have allergies to the device materials

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Valiant Navion™ Thoracic Stent Graft System Instructions for Use.

V. DEVICE DESCRIPTION

The Valiant Navion™ Thoracic Stent Graft System (also referred to as Valiant Navion Thoracic Stent Graft System) is comprised of two components:

- Valiant Navion stent graft
- Valiant Navion delivery system

The Valiant Navion stent graft is intended to be delivered endoluminally via access through the femoral or iliac artery to the site of the lesion using the Valiant Navion delivery system. The stent graft is inserted into and constrained by the delivery system outer sheath (graft cover). The pre-loaded stent graft is advanced to the lesion location over a guidewire. Upon deployment, the stent graft self-expands due to the superelastic properties of the nitinol stents. The proximal and distal ends of the stent graft are intended to conform to the shape and size of the proximal and distal seal zones due to the radial force of the stents.

Valiant Navion Stent Graft

Valiant Navion stent graft is a self-expanding, tubular endoprosthesis composed of polyester graft fabric and a stent scaffold made from nitinol wire. The metal scaffolding is composed of a series of sinusoidal stents stacked in a tubular configuration. Non-resorbable sutures attach the stents to the polyester fabric.

Platinum-Iridium radiopaque (RO) markers are sewn to the fabric to allow radiographic visualization of the edges of the graft material, and to provide a guide to the minimum overlap distance required when multiple stent grafts are used. The three proximal spherical markers and the two distal spherical markers indicate the extremities of the covered stent graft. The mid graft marker indicates a potential overlap edge, in the event additional stent grafts are used. The RO markers are at the same location and have the same configuration in all the Valiant Navion stent graft configurations.

A single, primary Valiant Navion stent graft may be used by itself if its length is sufficient to provide the desired coverage. Alternatively, it may be used in combination with additional Valiant Navion stent graft configurations that increase the graft length distally or proximally to the primary section.

The Valiant Navion stent graft is available in four configuration options:

- FreeFlo Straight

  The FreeFlo Straight configuration stent grafts are available in diameters ranging from 20 mm to 46 mm and covered lengths of approximately 60mm, 100 mm, 175 mm, and 225 mm.

- FreeFlo Tapered

  The FreeFlo Tapered configurations are available in proximal diameters ranging from 25 mm to 46 mm and distal diameters ranging from 20 mm to 40 mm. The covered length is approximately 175 mm with a stent graft taper of 5 mm for the smallest diameter configuration and 6 mm for the remaining sizes.

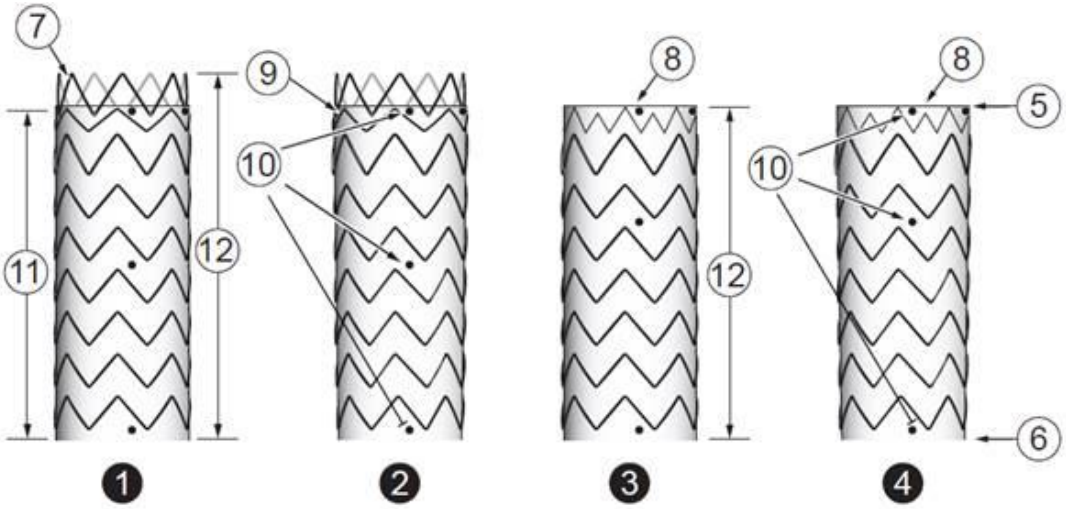
- CoveredSeal Straight

  The CoveredSeal Straight configuration stent grafts are available in diameters ranging from 20 mm to 46 mm and covered lengths of approximately 60mm, 100 mm, 175 mm, and 225 mm.

- <u>CoveredSeal Tapered</u>
  The CoveredSeal Tapered configurations are available in proximal diameters ranging from 25 mm to 46 mm and distal diameters ranging from 20 mm to 40 mm. The covered length is approximately 175 mm and 200 mm with a stent graft taper of 5 mm for the smallest diameter configuration and 6 mm for the remaining sizes.

See **Figure 1** below for the drawing of the four stent graft configurations of the Valiant Navion Thoracic Stent Graft System.

Figure 1: Stent Graft Configuration Components



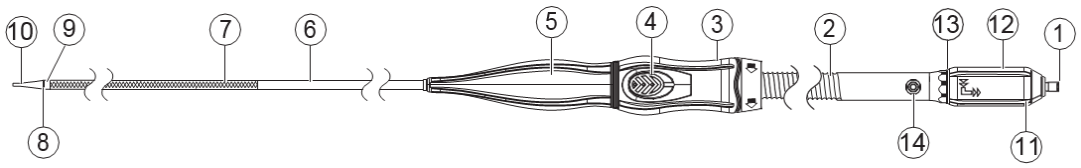
1. FreeFlo Straight
2. FreeFlo Tapered
3. CoveredSeal Straight
4. CoveredSeal Tapered
5. Proximal end
6. Distal end
7. FreeFlo stent
8. Internal stent
9. Support stent
10. RO marker
11. Covered length
12. Total length

<u>Valiant Navion Delivery System</u>

The Valiant Navion delivery system consists of a single-use, disposable catheter with an integrated handle, intended to provide controlled deployment. It is available in an outer diameter of 18, 20, and 22 Fr and a working length of 93 cm. The catheter assembly is flexible and exclusively compatible with a 0.035 in (0.89 mm) guidewire. A flexible tapered tip is attached to the end of the inner member and provides a smooth transition from the guidewire to the outer graft cover. The external surfaces of the tapered tip and graft cover are coated with a lubricious hydrophilic coating. Once activated with a sterile gauze

saturated in saline, this coating facilitates vessel access and tracking through the anatomy. A distal RO marker indicates the graft cover edge under fluoroscopy. The flush port includes a one-way valve that prevents backflow of flush fluid and maintains hemostasis during the procedure, while allowing the delivery system to be flushed during device preparation. The stent graft is deployed by rotating or retracting the integrated slider handle. The tip capture release handle at the rear of the delivery system is unlocked and retracted to release the proximal end of the stent graft.

Figure 2: Delivery System Components



1. Luer connector
2. Screw gear
3. Slider handle
4. Trigger
5. Front grip
6. Graft cover
7. Stent stop
8. Tip capture mechanism
9. RO marker band
10. Tapered tip
11. Back-end lock
12. Tip capture release handle
13. Clamping ring
14. Flush port

For additional details on the Valiant Navion Thoracic Stent Graft System, refer to the Valiant Navion Thoracic Stent Graft System Instructions for Use.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for the treatment of lesions of the descending thoracic aorta including medical management, open surgical repair, and endovascular repair using another endovascular grafting system. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Valiant Navion Thoracic Stent Graft System has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device provided from the Valiant Navion Thoracic Stent Graft System Instructions for Use.

Access failure	Embolism	Procedural bleeding
Access site complications (for example, spasm, trauma, bleeding, rupture, dissection)	Endoleaks	Prosthesis dilatation
Adynamic ileus	Excessive or inappropriate radiation exposure	Prosthesis infection
Allergic reaction (to contrast, antiplatelet therapy, stent graft material)	Extrusion/erosion	Prosthesis rupture
Amputation	Failure to deliver the stent graft	Prosthesis thrombosis
Anaphylaxis	Femoral neuropathy	Pseudoaneurysm
Anesthetic complications	Fistula (including aortobronchia, aortoenteric, aortoesophogeal, arteriovenous, and lymph)	Pulmonary edema
Aneurysm rupture	Gastrointestinal bleeding/complications	Pulmonary embolism
Angina	Genitourinary complications	Reaction to anaesthesia
Aortic expansion (for example: aneurysm, false lumen)	Hematoma	Renal failure
Aortic valve damage	Hemorrhage/bleeding	Renal insufficiency
Aortic vessel rupture	Hypotension/hypertension	Reoperation
Arrhythmia	Infection or fever	Respiratory depression or failure
Arterial stenosis	Insertion or removal difficulty	Retrograde type A dissection
Atelectasis	Intercostal pain	Sepsis
Balloon rupture	Intramural hematoma	Seroma
Blindness	Leg edema/foot edema	Sexual dysfunction
Bowel ischemia	Loss of patency	Shock
Bowel necrosis	Lymphocele	Spinal neurological deficit
Bowel obstruction	Myocardial infarction	Stenosis
Branch vessel occlusion	Neck enlargement	Stent graft migration
Breakage of the metal portion of the device	Nerve injury	Stent graft misplacement
Buttock claudication	Neuropathy	Stent graft occlusion

Cardiac tamponade	Occlusion - Venous or Arterial	Stent graft rupture (for example: holes, tears)
Catheter breakage	Pain/reaction at catheter insertion site	Stent graft twisting or kinking
Cerebrovascular accident (CVA)/Stroke	Paralysis	Transient ischemic attack (TIA)
Change in mental status	Paraparesis	Thrombosis
Coagulopathy	Paraplegia	Tissue necrosis
Congestive heart failure	Paresthesia	Vascular ischemia
Contrast toxicity	Perfusion of the false lumen	Vascular trauma
Conversion to surgical repair	Peripheral ischemia	Wound dehiscence
Damage to the vessel	Peripheral nerve injury	Wound healing complications
Death	Pneumonia	Wound infection
Deployment difficulties/failures	Postimplant syndrome	
Dissection, perforation, or rupture of the aortic vessel & surrounding vasculature	Post-procedural bleeding	

For the specific adverse events that occurred in the clinical study, please see **Section X** below.

IX. SUMMARY OF NONCLINICAL STUDIES

The following nonclinical studies were performed on the Valiant Navion Thoracic Stent Graft System:

A. Biocompatibility Testing
B. *In Vitro* Bench Testing
C. Sterilization, Packaging, and Shelf Life
D. Animal Studies

A. Biocompatibility Testing

Biocompatibility testing was conducted on materials in the Valiant Navion Thoracic Stent Graft System in accordance with Good Laboratory Practice for Non clinical Laboratory Studies (21 CFR 58). The test strategy and biological end point requirements were selected in consideration of the following standard/ guidances:

- International Standard ISO 10993-1, Biological Evaluation of Medical Devices
- YAKUSHOKUKIHATSU No. 0301-20: 2012, Requirements specified by the Japanese Ministry of Health, Labour, and Welfare (MHLW)

Table 1 and **Table 2** summarize the biocompatibility test results for the Valiant Navion stent graft and Valiant Navion delivery system, respectively.

Test methods were performed in accordance with the following, as referenced:

- ISO 10993-3: Tests for genotoxicity, carcinogenicity, and reproductive toxicity
- ISO 10993-4: Selection of tests for interactions with blood
- ISO 10993-5: Tests for *in vitro* cytotoxicity
- ISO 10993-6: Tests for local effects after implantation
- ISO 10993-10: Tests for irritation and skin sensitization
- ISO 10993-11: Tests for systemic toxicity
- YAKUSHOKUKIHATSU No. 0301-20: 2012, Requirements specified by the Japanese Ministry of Health, Labour, and Welfare (MHLW)
- United States Pharmacopeia (USP) 38, National Formulary (NF) 33, General Chapter <151>, Pyrogen Test
- American Society for Testing and Materials (ASTM) F756, Standard Practice for Assessment of Hemolytic Properties of Materials
- American Society for Testing and Materials (ASTM) F2382, Standard Test Method for Assessment of Intravascular Medical Device Materials on Partial Thromboplastin Time (PTT)

Table 1: Biocompatibility Test Results for Valiant Navion Stent Graft

Test Method	Test Purpose	Acceptance Criteria	Results
Cytotoxicity Study Using the Colony Assay (Extraction Method) – ISO 10993-5 and MHLW	To evaluate the potential for leaching substances from the test article to produce cytotoxicity by measuring the effect on colony formation of Chinese hamster lung cells (V79-4).	An IC_{50} of 100% or more indicates no/very weak cytotoxicity; IC_{50} weaker than Positive Control B indicates weak cytotoxicity; IC_{50} midway between Positive Control A and Positive Control B indicates moderate cytotoxicity; IC_{50} stronger than Positive Control A indicates severe cytotoxicity. A cytotoxic response was determined as a 30% or greater reduction in colonies as compared to the reagent control.	Pass
Cytotoxicity Study Using the ISO 10993-5 Direct Contact Method	To evaluate the cytotoxicity of a test article using an *in vitro* mammalian cell culture test.	The test article must result in a grade 2 or less.	Pass
Cytotoxicity Study Using the ISO 10993-5 Elution Method	To determine whether leachables extracted from the test article would cause cytotoxicity.	The test article must result in a grade 2 or less.	Pass
Guinea Pig Maximization Sensitization Test – ISO 10993-10	To evaluate the potential of the test article to cause delayed dermal contact sensitization in the guinea pig maximization test.	A grade of ≥ 1 in the test group indicates sensitization provided the corresponding control group is graded < 1.	Pass

Test Method	Test Purpose	Acceptance Criteria	Results
Intracutaneous Study in Rabbits – ISO 10993-10	To evaluate the local dermal irritation of a test article extract following intracutaneous injection in rabbits.	The difference between the test extract mean score and the corresponding control mean score must be 1.0 or less.	Pass
Systemic Toxicity Study in Mice, MHLW and ISO10993-11	To evaluate acute systemic toxicity of a test article extract following a single intravenous or intraperitoneal injection in mice.	If during the observation period none of the test animals show a significantly greater reaction than the corresponding control animals, the test article meets the test requirements.	Pass
Systemic Toxicity in Rats Following Subcutaneous Implantation, 4 Weeks – ISO 10993-11 and ISO 10993-6	To evaluate the potential for systemic toxicity of the test article following subcutaneous implantation in the rat for up to 4 weeks. The local tissue response to the test article at the implantation sites was also evaluated.	Body weight, organ weight, organ/body and organ/brain weight ratios, hematology, and clinical chemistry data will be evaluated statistically. Male and female data will be analyzed separately. Calculations resulting in p-values < 0.05 will be considered statistically significant. In the event of statistical significance for any hematologic parameter, the results may be compared to a reference range to determine biological significance. A pathologist will conduct a subjective microscopic evaluation of changes in tissues using a scoring scheme from 1 (minimal) to 4 (marked). The tissues will be evaluated for evidence of toxicity. Microscopic evaluation of the implant sites will be graded based on ISO, with the scores of the test article sites compared to the control article sites.	Pass
Systemic Toxicity Study in Rats Following Subcutaneous Implantation, 13 Weeks – ISO 10993-11 and ISO 10993-6	To evaluate the potential for systemic toxicity of the test article following subcutaneous implantation in the rat for up to 13 weeks. The local tissue response to the test article at the implantation sites was also evaluated.	Body weight, organ weight, organ/body and organ/brain weight ratios, hematology, and clinical chemistry data will be evaluated statistically. Male and female data will be analyzed separately. Calculations resulting in p-values < 0.05 will be considered statistically significant. In the event of statistical significance for any	Pass

Test Method	Test Purpose	Acceptance Criteria	Results
		hematologic parameter, the results may be compared to a reference range to determine biological significance. A pathologist will conduct a subjective microscopic evaluation of changes in tissues using a scoring scheme from 1 (minimal) to 4 (marked). The tissues will be evaluated for evidence of toxicity. Microscopic evaluation of the implant sites will be graded based on ISO, with the scores of the test article sites compared to the control article sites.	
Rabbit Pyrogen Study, Material Mediated - USP38-NF33<151> and ISO 10993-11	To determine whether an extract of the test article induced a pyrogenic response following intravenous injection in rabbits.	If no animal shows an individual rise in temperature of 0.5°C or more above its baseline temperature, the test article meets the requirements for the absence of pyrogens.	Pass
Bacterial Reverse Mutation Study – ISO 10993-3	To evaluate whether a test article extract would cause mutagenic changes in *Salmonella typhimurium* tester strains TA98, TA100, TA1535, and TA1537, and *Escherichia coli* tester strain WP2*uvrA* in the presence and absence of mammalian metabolic activation.	For the test article to be identified as a potential mutagen, there must be a 2-fold or greater increase in the number of mean revertants over the means obtained from the negative control for strains TA98, TA100, and WP2*uvrA*. For the test article to be identified as a potential mutagen there must be a 3-fold or greater increase in the number of mean revertants over the means obtained from the negative control for strains TA1535 and TA1537.	Pass
Mouse Lymphoma Assay – ISO 10993-3	To evaluate whether the test article extract induced gene mutations and chromosomal damage in mammalian cells.	The test article will be evaluated as positive if there is a two-fold or greater increase in mean mutation frequency over the mean background mutation frequency of the negative (vehicle) control. The test article will be evaluated as negative if a two-fold increase is not observed. The test article will be evaluated as equivocal if there is no consistent evidence for either	Pass

Test Method	Test Purpose	Acceptance Criteria	Results
		a positive or negative evaluation.	
Mouse Peripheral Blood Micronucleus Study – ISO 10993-3	To evaluate the potential for a test article extract to cause damage to chromosomes or the mitotic apparatus of murine erythroblasts by measuring the frequency of micronucleated reticulocytes (MN-RETs) in mice.	The test article will be evaluated as positive if there is a two-fold or greater increase in mean mutation frequency over the mean background mutation frequency of the negative (vehicle) control. The test article will be evaluated as negative if a two-fold increase is not observed. The test article will be evaluated as equivocal if there is no consistent evidence for either a positive or negative evaluation.	Pass
Hemolysis Study – ASTM F756 and ISO 10993-4	To determine whether the test article would cause hemolysis *in vitro* by direct contact or extraction.	Resulting hemolytic index of ≤ 2% will be considered non-hemolytic, 2 to 5% will be considered slightly hemolytic, and > 5% will be considered hemolytic. A resulting hemolytic index of ≤ 5% will be considered acceptable.	Pass
Complement Activation, C3a – ISO 10993-4	To determine the complement activation potential of the test article using an *in vitro* system.	If the C3a concentration in the test article is statistically similar to at least the negative control, activated normal human serum (NHS), or the sponsor-provided control, the test article is not considered an activator of the complement system. If the C3a concentration in the test article is not statistically similar to any of the aforementioned controls, an evaluation with regards to overall patient safety will be completed.	Pass
Complement Activation, SC5b-9 – ISO 10993-4	To determine the potential of the test article to activate the complement system.	If the SC5b-9 concentration in the test article is statistically similar to at least the negative control, activated NHS, or the sponsor-provided control, the test article is not considered an activator of the complement system. If the SC5b-9 concentration in the test article is not statistically similar to any of the aforementioned controls, an evaluation with regards to overall patient safety will be completed.	Pass
Partial Thromboplastin	To determine the potential of	% of negative control > 50%	Pass

Test Method	Test Purpose	Acceptance Criteria	Results
Time – ASTM F2382 and ISO 10993-4	the test article to cause an effect on the coagulation cascade via the intrinsic coagulation pathway.	is considered acceptable per ASTM F2382.	
In vivo thromboresistance – ISO 10993-4	To evaluate relative thromboresistance of the test article *in vivo*.	Thrombi formation will be scored 0 (No significant thrombosis) to 5 (Vessel completely occluded). The test article must score better or similarly when compared to the commercially approved sponsor-provided control article.	Pass

Table 2: Biocompatibility Test Results for Valiant Navion Delivery System

Test Method	Test Purpose	Acceptance Criteria	Results
Cytotoxicity Study Using the ISO 10993-5 Elution Method	To determine whether leachables extracted from the test article would cause cytotoxicity.	The test article must result in a grade 2 or less.	Pass
Guinea Pig Maximization Sensitization Test – ISO 10993-10	To evaluate the potential of the test article to cause delayed dermal contact sensitization in the guinea pig maximization test.	A grade of ≥ 1 in the test group indicates sensitization provided the corresponding control group is graded < 1.	Pass
Intracutaneous Study in Rabbits – ISO 10993-11	To evaluate the local dermal irritation of a test article extract following intracutaneous injection in rabbits.	The difference between the test extract mean score and the corresponding control mean score must be 1.0 or less.	Pass
Systemic Toxicity Study in Mice – ISO 10993-11	To determine whether leachables extracted from the test article would cause acute systemic toxicity following injection into mice.	If during the observation period none of the test animals show a significantly greater reaction than the corresponding control animals, the test article meets the test requirements.	Pass
Rabbit Pyrogen Study, Material Mediated – USP38-NF33<151> and ISO 10993-11	To determine whether an extract of the test article induced a pyrogenic response following intravenous injection in rabbits.	If no animal shows an individual rise in temperature of 0.5°C or more above its baseline temperature, the test article meets the requirements for the absence of pyrogens.	Pass

Test Method	Test Purpose	Acceptance Criteria	Results
Bacterial Reverse Mutation Study – ISO 10993-3	To evaluate whether a test article extract would cause mutagenic changes in *Salmonella typhimurium* tester strains TA98, TA100, TA1535, and TA1537, and *Escherichia coli* tester strain WP2*uvrA* in the presence and absence of mammalian metabolic activation.	For the test article to be identified as a potential mutagen there must be a 2-fold or greater increase in the number of mean revertants over the means obtained from the negative control for strains TA98, TA100, and WP2*uvrA*. For the test article to be identified as a potential mutagen there must be a 3-fold or greater increase in the number of mean revertants over the means obtained from the negative control for strains TA1535 and TA1537.	Pass
Mouse Lymphoma Assay – ISO 10993-3	To evaluate whether the test article extract induced gene mutations and chromosomal damage in mammalian cells.	The test article will be evaluated as positive if there is a two-fold or greater increase in mean mutation frequency over the mean background mutation frequency of the negative (vehicle) control. The test article will be evaluated as negative if a two-fold increase is not observed. The test article will be evaluated as equivocal if there is no consistent evidence for either a positive or negative evaluation.	Pass
Hemolysis Study – ASTM F756 and ISO 10993-4	To determine whether the test article would cause hemolysis *in vitro* by direct contact or extraction.	Resulting hemolytic index of ≤ 2% will be considered non-hemolytic, 2 to 5% will be considered slightly hemolytic, and > 5% will be considered hemolytic. A resulting hemolytic index of ≤ 5% will be considered acceptable.	Pass
C3a Complement Activation Assay – ISO 10993-4	To determine the complement activation potential of the test article using an *in vitro* system.	If the C3a concentration in the test article is statistically similar to at least the negative control, activated NHS, or the sponsor-provided control, the test article is not considered an activator of the complement system. If the C3a concentration in the test article is not statistically similar to any of the aforementioned controls, an evaluation with regards to overall patient safety will be completed.	Pass

Test Method	Test Purpose	Acceptance Criteria	Results
SC5b-9 Complement Activation Assay – ISO 10993-4	To determine the potential of the test article to activate the complement system.	If the SC5b-9 concentration in the test article is statistically similar to at least the negative control, activated NHS, or the sponsor-provided control, the test article is not considered an activator of the complement system. If the SC5b-9 concentration in the test article is not statistically similar to any of the aforementioned controls, an evaluation with regards to overall patient safety will be completed.	Pass
Partial Thromboplastin Time – ASTM F2382 and ISO 10993-4	To determine the potential of the test article to cause an effect on the coagulation cascade via the intrinsic coagulation pathway.	% of negative control > 50% is considered acceptable per ASTM F2382.	Pass
In Vivo Thromboresistance Study in Swine – ISO 10993-4	To evaluate relative thromboresistance of the materials *in vivo*.	Thrombi formation will be scored 0 (No significant thrombosis) to 5 (Vessel completely occluded). The test article must score better or similarly when compared to the commercially approved sponsor-provided control article.	Pass

B. ***In Vitro* Bench Testing**

In vitro design verification and validation testing of the Valiant Navion Thoracic Stent Graft System was carried out to determine whether the design met all associated Product Performance Specifications and to confirm similar *in vitro* performance to the Valiant® Thoracic Stent Graft with the Captivia® Delivery System (also referred to as the Valiant Captivia Thoracic Stent Graft System). Testing was conducted on a subset of device configurations/sizes representative of the entire catalog or worst-case for each test, as appropriate to represent the entire device range available with the Valiant Navion Thoracic Stent Graft System. All *in vitro* bench tests produced acceptable results.

Bench testing was performed per Medtronic Vascular test protocols which incorporated the requirements of the international standard BS EN ISO 25539-1:2017 *Cardiovascular Implants – Endovascular Devices – Part 1: Endovascular Prostheses*. The testing details include results from T=0 (baseline) as well as results using samples accelerated aged to 2 years (T=2). An asterisk (*) indicates testing was performed at both T=0 and T=2. A summary of the *in vitro* testing is provided in **Table 3**. Results obtained from *in vitro* testing provided evidence supporting the safety and effectiveness of the Valiant Navion Thoracic Stent Graft System.

Table 3: Summary of Tests Performed Related to Functionality of the Valiant Navion Thoracic Stent Graft System

***In Vitro* Test**	**Test Purpose**	**Acceptance Criteria**	**Results**
Crossing Profile*	To assess the maximum outside diameter of the delivery system.	Appropriate ring gauge must pass over the loaded delivery system per the table below: **Catheter Size** / **Crossing Profile (OD, max)** 18 Fr / 6.17 mm 20 Fr / 6.83 mm 22 Fr / 7.50 mm	Pass
Delivery System Dimensional Verification*	To determine the working length and the hydrophilic length of the delivery system.	Working Length = 93 ± 2 cm Hydrophilic Coating Length > 80 cm	Pass
Stent Graft Dimensional Verification Post Deployment (Outer Diameter)*	To measure the diameter of a Valiant Navion stent graft post deployment.	Diameter ≥ (Labeled Nominal Diameter – 1 mm)	Pass
Stent Graft Dimensional Verification Post Deployment (Length)*	To measure the stent graft length post deployment.	Covered Stent Graft Length = **Nominal (mm)** / **Tolerance (mm)** 60 / +3 / -6 100 / +5 / -10 175 / +10 / -15 200 / +10 / -15 225 / +10 / - 20	Pass
Delivery System Hemostasis*	To determine the hemostatic flow rate of the delivery system when pressurized to physiologic conditions.	Water flow rate < 6.5 mL/min	Pass
Graft Cover to Radiopaque Marker Bond Strength*	To determine the maximum load required to break the bond between the graft cover and radiopaque (RO) marker of the delivery system.	Ultimate Tensile Strength Lower Tolerance Limit (LTL) > 0.5 * Net Deployment Force UTL	Pass
Graft Cover T-tube Tensile Strength*	To determine the maximum load required to break the bond between the graft cover and graft cover T-tube overmold of the delivery system.	Ultimate Tensile Strength LTL > Net Deployment Force UTL	Pass
Graft Cover Yield Strength*	To determine the midpoint yield strength of the graft cover of the delivery system.	Midpoint Yield Strength LTL > Net Deployment Force UTL	Pass

In Vitro Test	Test Purpose	Acceptance Criteria	Results
Graft Cover Bond Strength*	To determine the maximum load required to break the bond between the two sections of the delivery system graft cover.	Yield Strength LTL > Net Deployment Force UTL	Pass
Graft Cover T-Tube Torque Strength*	To determine the maximum torque required to break the bond between the graft cover and graft cover T-tube overmold of the delivery system.	Ultimate Torque Strength LTL > 0.183 N-m	Pass
Front Grip Tensile Strength*	To measure the maximum load required to separate the front grip from the delivery system handle.	Ultimate Tensile Strength LTL > Deployment Force UTL	Pass
Tip Assembly to Guidewire Lumen Bond Tensile*	To determine the maximum load required to break the bond between the tapered tip and guidewire tube of the delivery system.	Ultimate Tensile Strength LTL > 44N	Pass
Spindle to Tapered Tip Tensile Strength*	To determine the maximum load required to break the bonds between the spindle, tapered tip insert, and the tapered tip of the delivery system.	Ultimate Tensile Strength LTL > 44N	Pass
Capture Fitting Tensile*	To determine the maximum load required to break the bond between the capture fitting and guidewire tube of the delivery system.	Ultimate Tensile Strength LTL > Net Tip Release Force UTL	Pass
Flush Port to Hypotube Tensile Strength*	To determine the maximum load required to break the bond between the flush port and hypotube of the delivery system.	Ultimate Tensile Strength LTL > 22 N	Pass
Middle Member to Flush Port Seal Compression*	To determine the maximum load required to compress the middle member by a set distance into the flush port seal of the delivery system.	Ultimate Compression LTL > UTL Net Deployment Force * 0.75	Pass
Middle Member to Flush Port Seal Tensile*	To determine the maximum load required to separate the middle member from the flush port seal in the delivery system.	Ultimate Tensile Strength LTL > 22N	Pass
Middle Member to Flexible Stent Stop Bond Strength*	To determine the maximum load required to break the bond between the middle member and flexible stent stop of the delivery system.	Ultimate Tensile Strength LTL > 22N	Pass

In Vitro Test	Test Purpose	Acceptance Criteria	Results
Middle Member to Extension Tube Bond Strength*	To determine the maximum load required to break the bond between the middle member and extension tube of the delivery system.	Ultimate Tensile Strength LTL > 15N	Pass
Middle Member to Sleeve Bond Strength*	To determine the maximum load required to break the bond between the middle member and sleeve of the delivery system.	Ultimate Tensile Strength LTL > 22 N	Pass
Backend Fitting Assembly Tensile*	To determine the maximum load required to break the bond between the backend fitting and guidewire tube of the delivery system.	Ultimate Tensile Strength LTL > 40N	Pass
Tip Release Fitting Assembly Tensile Strength*	To determine the maximum load required to break the bond between the tip release fitting and capture tube of the delivery system.	Ultimate Tensile Strength LTL > Tip release force UTL	Pass
T-Tube Seal Retainer Tensile Strength*	To determine the maximum load required to separate the T-tube seal retainer from the graft cover T-tube of the delivery system.	Ultimate Tensile Strength LTL > 22N	Pass
Screw Gear Disengagement Force*	To measure the force required to make the delivery system graft cover retractor skip over threads on a screw gear assembly.	Disengagement Force LTL > Deployment Force UTL	Pass
Spring Attachment Strength*	To test the attachment strength of the springs to the stent graft.	Spring Attachment Strength LTL > 133 N	Pass
Stent Graft Permeability	To determine the rate of water leakage through the stent graft.	Integral Water Permeability < 575 mL/min/cm^2	Pass
Stent Graft Burst*	To determine the pressure required to burst the stent graft.	Stent Graft Burst Pressure LTL > 120 kPA	Pass

In Vitro Test	Test Purpose	Acceptance Criteria	Results
Deployment Force*	To evaluate the forces required to release the stent graft from the delivery system in a simulated use model.	Deployment Force UTL < Lowest LTL of the following: Screw Gear Disengagement Force Front Grip Tensile Strength and Net Deployment Force UTL* < Lowest LTL of the following: Graft Cover Yield Strength Graft Cover Bond Strength Graft Cover T-Tube Tensile Strength 0.5 * Net Deployment Force UTL < Graft Cover to Radiopaque Marker Bond Strength LTL 0.75 * Net Deployment Force UTL < Middle Member to Flush Port Seal Compression LTL	Pass
Tip Release Force*	To evaluate the forces required to release the proximal end of the stent graft from the delivery system in a simulated use model.	Tip Release Force UTL < Tip Release Fitting Assembly Tensile Strength LTL Net Tip Release Force UTL < Capture Fitting Tensile Strength LTL	Pass
Stent Graft Body Conformability	To assess flexibility by measuring diameter reduction in the stent graft when placed at an angle of 90º.	Cross-sectional area of stent graft in 90° bend > 50% of cross-sectional area of stent graft at 0°	Pass
Stent Graft Radial Pressure	To determine the radial force exerted by the stent graft in the seal zones during radial compression consistent with anticipated clinical operating conditions.	Seal zone radial pressure > 8.0 mm Hg	Aneurysm: Pass Transection: Pass

In Vitro Test	Test Purpose	Acceptance Criteria	Results
Stent Graft Joint Strength	To evaluate the joint strength between stent graft components.	Joint strength greater than or equal to previous generation device results, at a 95% level of confidence: • Ho: Valiant Navion stent graft results are >/= Valiant Captivia stent graft results, • Ha: Valiant Navion stent graft results are < Valiant Captivia stent graft results.	Pass
Stent Graft Proximal Seal	This test evaluates the amount of water leakage at the stent graft seal zones.	Leak Rate results must be less than or equal to previous generation device results, at a 95% level of confidence: • Ho: Valiant Navion stent graft results are >/= Valiant Captivia stent graft results, • Ha: Valiant Evo stent graft results are < Valiant Captivia stent graft results.	Pass
Stent Graft Migration	To measure the maximum pressure that a stent graft can withstand before migrating through a mock vessel over an intended landing zone length.	Migration Pressure results must be greater than or equal to previous generation device results, at a 95% level of confidence: • Ho: Valiant Navion stent graft results are ≥ Valiant Captivia stent graft results • Ha: Valiant Navion stent graft results are < Valiant Captivia stent graft results.	Pass
Stent Graft Proximal Conformability	To evaluate the extent of bird beaking (i.e. lack of wall apposition against the inner curve of the aortic arch) exhibited by the proximal end of the stent graft.	Bird beak covered length must be less than or equal to previous generation device results, at a 95% level of confidence: • Ho: Valiant Navion stent graft results are ≥ Valiant Captivia stent graft results • Ha: Valiant Navion stent graft results are < Valiant Captivia stent graft results.	Pass

***In Vitro* Test**	**Test Purpose**	**Acceptance Criteria**	**Results**
Stent Graft Visual Expansion Integrity*	To assess the visual expansion integrity of the stent graft.	1. No broken or bent stent struts including crimp sleeve. 2. No graft hole(s) with area > 0.2 mm^2. 3. No stitch breaks permitted on Internal or Bare stent struts. Stitch breaks are acceptable at other stent locations provided that the minimum number of stitches are met. Stitch breaks on seam are acceptable provided that the minimum stitch density of 12 stiches/cm is maintained 1 cm on each side of the break. 4. Loose or frayed sutures are acceptable if the stent and/or RO marker remains attached to the graft material. 5. RO markers must remain attached to the stent graft.	Pass
Guidewire Acceptance*	To confirm that the delivery system accepts a 0.035" guidewire.	A 0.035" (0.89 mm) guidewire must be able to pass/track through the delivery system.	Pass
Finite Element Analysis	To calculate fatigue safety factors by quantifying the strain on the stent when subject to *in vivo* conditions.	The safety factors based on the endurance limit shall be > 1.	Pass

***In Vitro* Test**	**Test Purpose**	**Acceptance Criteria**	**Results**
MRI	To evaluate MRI compatibility with the stent graft.	1. The device must be MR Conditional with respect to implant radiofrequency (RF) heating in a 1.5T and 3T system. 2. The magnetically induced deflection force is less than the force on the stent due to gravity (its weight). 3. The stent graft with the greatest clinically relevant metallic mass must exhibit insufficient magnetic torque in a 3.0-Tesla MRI system to align with the magnetic field when resting on a hard-smooth surface at the magnetic isocenter. 4. Characterize image artifact	Pass
Cyclic Potentiodynamic Polarization (Corrosion)	To evaluate the susceptibility of the stent rings to corrosion in a simulated physiological environment.	$E_b - E_r > 200mV$	Pass

***In Vitro* Test**	**Test Purpose**	**Acceptance Criteria**	**Results**
Supported Single Layer Radial Dilatation Fatigue	To evaluate the device durability of a single layer of the stent graft following 10 years simulated (400 million cycles) accelerated *in vitro* testing under clinically-relevant loading conditions.	Each test sample must meet performance requirements of stent, graft material, and suture components after completing 400 million cycles of radial dilation fatigue testing. Stent: No CoveredSeal support stent fractures that result in the complete detachment of stent fragments from the stent graft. No stent fractures of all other stents. Graft material: Graft hole effective area must be less than or equal to 5.7 mm^2. Graft material for Transection Indication evaluated based on performance requirement of 40 million cycles (1 -Year equivalent) Suture: No suture breaks that result in the complete detachment of a stent or radiopaque marker.	Pass
Supported Overlap Radial Dilatation Fatigue	To evaluate the device durability of overlapped stent grafts within a supported, simulated vessel region following 10 years simulated (400 million cycles) accelerated *in vitro* testing under clinically-relevant loading conditions.	Each test sample must meet performance requirements of stent, graft material, and suture components after completing 400 million cycles of overlap radial dilation fatigue testing Stent: No CoveredSeal support stent fractures that result in the complete detachment of stent fragments from the stent graft. No stent fractures of all other stents. Graft material: Graft hole effective area must be less than or equal to 5.7 mm^2. Suture: No suture breaks that result in the complete detachment of a stent or radiopaque marker	Pass

In Vitro Test	Test Purpose	Acceptance Criteria	Results
Unsupported Pulsatile Fatigue	To evaluate the device durability in an unsupported environment (simulating an aneurysm sac) following 10 years simulated (400 million cycles) accelerated *in vitro* testing under clinically-relevant loading conditions.	Each test sample must meet performance requirements of stent, graft material, and suture components after completing 400 million cycles of unsupported pulsatile fatigue testing Stent: No CoveredSeal support stent fractures that result in the complete detachment of stent fragments from the stent graft. No stent fractures of all other stents. Graft material: Graft hole effective area must be less than or equal to 1.7 mm^2 . Suture: No suture breaks that result in the complete detachment of a stent or radiopaque marker	Pass
Simulated Use	For experienced physicians to evaluate the stent graft system's ability to perform in a simulated clinical environment.	Successfully meet performance requirements as the steps of the IFU are executed in a simulated clinical environment. The following attributes were evaluated to determine whether "clinically acceptable": • Guidewire compatibility • Ability to flush • Ancillary compatibility • Hydrocoating is activated • Ability to access • Visbility • Ability to accurately deploy and re-position • Fixation effectiveness • Iliac access • Ease of Use • Ability to withdraw • Troubleshooting techniques	Pass
LTL denotes Lower Tolerance Limit; UTL denotes the Upper Tolerance Limit.			

C. Sterilization/Packaging/Shelf Life

The Valiant Navion Thoracic Stent Graft System is a single-use device that is provided sterile to the end user. The device is sterilized using E-Beam sterilization and is validated to demonstrate a Sterility Assurance Level (SAL) of 10^{-6}.

Packaging performance and stability testing demonstrate that the packaging designs for the Valiant Navion Thoracic Stent Graft System are sufficient to adequately protect the device and maintain the sterile integrity of the Valiant Navion Thoracic Stent Graft System package throughout its 2-year shelf-life claim.

Product shelf-life testing conducted on the Valiant Navion Thoracic Stent Graft System supports a 2-year shelf life claim. Shelf-life testing results are presented within the *in vitro* bench test results as part of **Table 3** above.

D. Animal Studies

Preclinical *in vivo* animal testing of the Valiant Navion Thoracic Stent Graft System was conducted to evaluate acute technical performance, stent graft integrity, and histopathological response of the Valiant Navion Thoracic Stent Graft System in an ovine model for up to 6 months. The results demonstrated an adequate ability to access the target anatomical location, adequate handling and visualization of the delivery system and implant, and adequate deployment accuracy. Stent graft integrity and histopathological response were acceptable. The 28-day, 60-day and 180-day results of the animal study support the safety of the Valiant Navion stent graft.

Table 4: Summary of the Animal Studies

Study Name/ Description and Sample Size	Evaluations	Outcome
28 and 60 Day Safety Evaluation in the Ovine Model One Valiant Navion Thoracic Stent Graft was placed in the thoracic aorta and one Endurant II Abdominal Stent Graft was placed in the abdominal aorta of each of 6 sheep for a total of 2 grafts per animal.	Acute Assessment: • Acute stent graft deployment, stent graft placement, and any device related effects at the time of implant. • Acute performance including: trackability, flexibility, pushability, kink resistance, atraumatic interface, and withdrawal of the Valiant Navion delivery system. • Compatibility of the delivery system with standard accessory products including guidewires, introducer sheaths, luer adapters and balloons. • Ability to inject contrast. • Visibility of the Valiant Navion Thoracic Stent Graft System under fluoroscopy for both stent graft and delivery system. • Functional hemostasis of delivery	• Acute delivery performance and compatibility with accessory devices was scored as "clinically acceptable" by the interventionalist, based on the interventionalist's clinical experience. • All stent grafts were successfully delivered to the intended location. • There was one substantiated migration of the test devices. The cause was inconclusive and attributed to limitations in the animal model. • All vessels remained patent throughout the course of the studies. • There was no evidence of stent fractures. • Comparable histological indicators of vessel wall healing, including evaluation of strut induced vessel wall injury, inflammation, thrombus,

Study Name/ Description and Sample Size	Evaluations	Outcome
	system. • Structural integrity of delivery system. • Evaluation of patency. • Ease of use, including ergonomics. Chronic Assessment: • Evaluation of the position of the implant at the time of implant and the time of explant (migration resistance). • Evaluation of patency. • Evaluation of the structural integrity of the Valiant Navion Stent Graft at the time of explant. • Evaluation of histology and pathology of explanted test and control articles and surrounding tissue.	endothelialization, and neointimal formation, was noted at 28 days and 60 days for each study respectively between the test and control articles. • Overall quantitative morphometric analysis of tissue sections from the native (non-stented) proximal and distal stented vessels and proximal bare spring of both test and control article, proximal support spring, middle, and distal portions of the stents showed that the response to the test device was comparable to the control article.
The 180 Day Safety Evaluation in the Ovine Model One Valiant Navion Thoracic Stent Graft was placed in the thoracic aorta and one Endurant II Abdominal Stent Graft was placed in the abdominal aorta of each of 8 sheep for a total of 2 grafts per animal.	Acute Assement: • Access and withdrawal of the delivery system. • Compatibility of the delivery system with standard accessory products including guidewires, introducer sheaths, luer adapters and balloons. • Acute stent graft deployment, stent graft placement, and any device related effects at the time of implants. • Ability to flush (guidewire lumen and graft cover) with saline (via syringe). • Visibility under fluoroscopy for both stent graft and the delivery system. • Functional hemostasis of delivery system (lack of bleed). • Structural integrity of the delivery system. • Evaluation of patency. • System ease of use. Chronic Assement: • Evaluation of the position of the implant at the time of implant, 28 ± 2 days and the time of explant (migration resistance). • Evaluation of patency at 28 ± 2 days and 180 days. • Evaluation of the structural integrity	• Acute delivery performance was scored as “clinically acceptable” by the interventionalist, based on the interventionalist’s clinical experience. • All stent grafts were successfully delivered to the intended location. • All vessels remained patent throughout the course of the study. • There was no evidence of stent fractures. • There were two cases of test article migration reported. The cause of both migrations was inconclusive and attributed to limitations of the animal model and the anatomical landmarks; these are not considered representative of the device performance in humans. • Comparable histological indicators of vessel wall healing, including strut induced vessel wall injury, inflammation, thrombus, endothelialization, and neointimal formation, was noted between the test and control articles. • Overall quantitative morphometric analysis of tissue sections from the native (non-stented) proximal and distal stented vessels and proximal bare spring of both test and control article, proximal support spring,

Study Name/ Description and Sample Size	Evaluations	Outcome
	of the Valiant Navion Thoracic Stent Graft System at the time of explant. • Evaluation of histology and pathology of explanted test and control articles and surrounding tissue.	middle, and distal portions of the stents showed that the response to test article was comparable to the control article.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of endovascular aneurysm repair with the Valiant Navion Thoracic Stent Graft Systemin the US, Canada, Denmark, Italy, France, Netherlands, and UK under IDE # G150251. Data from this clinical study were the basis for the panel-track PMA-S approval decision.

The Valiant Navion Thoracic Stent Graft System is Medtronic's next generation thoracic stent graft system, based on the previously approved Valiant Captivia Thoracic Stent Graft System. The changes were intended to increase the range of stent graft sizes offered (shorter and longer lengths, smaller diameter, and increased stent graft taper offered), reduce the delivery system profile (18 Fr, 20 Fr, and 22 Fr instead of 22 Fr, 24 Fr, and 25 Fr), allow for the use of the CoveredSeal configuration as either the proximal or the distal device (previous Closed Web configuration was limited to use as the distal device), and allow for controlled delivery of all configurations.

Because the Valiant Navion Thoracic Stent Graft System is expected to perform similarly to Valiant Captivia Thoracic Stent Graft System, the clinical study (Valiant Evo IDE study) was designed to confirm that the device design modifications did not negatively impact clinical performance. The study was limited to the use of the device for the treatment of descending thoracic aortic aneurysms (DTAA) and penetrating aortic ulcers (PAU). The results from this study, with consideration of the clinical data from the evaluation of the Valiant Captivia Thoracic Stent Graft System, in combination with the nonclinical testing, supports the broad indication of all lesions of the descending thoracic aorta (DTA). The aortic anatomy associated with descending thoracic aortic aneurysms is technically most challenging, making them suitable patients to evaluate acute outcomes per the objectives of the Valiant Evo IDE study. Patients with aneurysm have been shown to be a worst-case population for endovascular repair of the thoracic aorta through prior clinical experience from Valiant Captivia Thoracic Stent Graft System. The aneurysm disease state is worst case when compared to transection and dissection disease states because the aneurysm poses additional challenge for the delivery system in traversing the aneurysm to reach the deployment target and deploying accurately within the short landing zone proximal to the aneurysm.

Note: Information regarding the clinical evaluation of the Valiant Captivia Thoracic Stent Graft System to treat traumatic transections, acute complicated

dissections and DTAA can be found in the IFU for this device; Medtronic's VALOR II study (Section 6.3 of the Valiant Captivia Thoracic Stent Graft System IFU), Medtronic Dissection Trial (Section 6.1 of the Valiant Captivia Thoracic Stent Graft System IFU) and RESCUE study (Section 6.2 of the Valiant Captivia Thoracic Stent Graft System IFU).

Note: The Valiant Navion Thoracic Stent Graft System was called the Valiant Evo Thoracic Stent Graft System during the clinical study. Therefore, the device is referred to as the Valiant Evo Thoracic Stent Graft System in this clinical study summary.

A. Study Design

Patients were treated between March 2016 and October 2017. The database for this Panel Track Supplement reflected data collected through December 11, 2017 and included 87 patients. There were 31 investigational sites.

A total of 100 subjects were consecutively enrolled as part of the Valiant Evo IDE study. Data on the first 87 of these subjects are presented in this clinical study summary [52 US, 35 OUS (6 Canada, 1 Denmark, 11 Italy, 8 France, 4 Netherlands, 5 UK)]. These 87 subjects were recruited from 31 medical centers worldwide, with 18 of the clinical sites coming from the United States and 13 from Outside the United States (OUS) (2 Canada, 1 Denmark, 4 Italy, 3 France, 2 Netherlands, and 1 UK).

The study was a prospective, multi-center, single-arm cohort, open-label clinical study with a dichotomous study outcome based on the binomial distribution for hypothesis testing. The primary study endpoint, the proportion of subjects with access failures, deployment failures, and/or Major Device Effects (MDE) within 30 days post index procedure, is a dichotomous study outcome, and was tested against a performance goal of 16%:

H_0: $p \geq 16\%$ vs. H_a: $p < 16\%$

where p denotes the true event rate of the primary study endpoint in the target population. Thus, if the null hypothesis, H_0, was rejected at the one-sided 0.025 statistical significance level, the performance goal for the primary endpoint was reached. All other endpoints were analyzed descriptively, and the time to event was analyzed by the Kaplan-Meier method.

The total of 100 subjects ensured that 87 evaluable subjects were available at the 30-day primary endpoint for analysis. The sample size of 87 evaluable subjects provided 85% statistical power for the study hypothesis. The type I error was controlled with a one-sided 0.025 statistical significance level.

The Valiant Evo IDE study was monitored by an internal Medtronic Contract Research Organization. An Imaging Core Lab, Data Monitoring Committee (DMC)

and Clinical Events Committee (CEC), all managed by the independent Contract Research Organization, were established to independently evaluate subject health status, device performance, and identify any safety concerns regarding subjects' well-being. The Clinical Events Committee (CEC) met to adjudicate MDEs, unanticipated adverse device effects (UADEs), unanticipated serious adverse device effects (USADEs), deaths, and all aneurysm ruptures for the global cohort. The Data Monitoring Committee (DMC) met to evaluate safety data during the course of the clinical study. The central imaging core lab was used to provide independent evaluation of imaging findings.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Valiant Evo IDE study was limited to subjects who met the following inclusion criteria:

- ≥18 years old.
- Signed and dated the Informed Consent Form.
- Presented with a DTAA that was localized below the ostium of LSA and above the ostium of celiac trunk.
- Had a DTAA that was one of the following:
  - A fusiform aneurysm with a maximum diameter that:
    - was ≥ 50 mm and/or:
    - was > 2 times the diameter of the non-aneurysmal thoracic aorta and/or:
    - was < 50 mm and had grown ≥ 5 mm within previous 12 months
  - A saccular aneurysm or a penetrating atherosclerotic ulcer
- Anatomy met all the following anatomical criteria as demonstrated on contrast-enhanced CT and/or on contrast-enhanced MRA obtained within four months prior to implant procedure:
  - Proximal and distal non-aneurysmal aortic neck diameter measurements were ≥ 16 mm and ≤ 42 mm;
  - Proximal non-aneurysmal aortic neck length was ≥ 20 mm (for FreeFlo configuration) and ≥ 25 mm (for Closed Web[1] configuration) distal to the left common carotid artery (LCCA). Note: Proximal aortic neck length may include covering the LSA (with or without discretionary revascularization) when necessary to optimize device fixation and maximize aortic neck length. If occlusion of the LSA ostium was required to obtain adequate neck length for fixation and sealing, transposition or bypass to the LSA may have been warranted.
  - Distal non-aneurysmal aortic neck length was ≥ 20 mm

[1] Closed Web refers to CoveredSeal configurations used in the clinical trial.

- Adequate arterial access site or could tolerate a conduit that allowed endovascular access to the aneurysmal site with the delivery system of the appropriate sized device chosen for the treatment.

Subjects were not permitted to enroll in the Valiant Evo IDE study if they met any of the following exclusion criteria:

- Life expectancy of <1 year.
- Participating in another investigational drug or device study that would interfere with the endpoints and follow-ups of this study.
- Currently pregnant.
- Required planned placement of the covered proximal end of the stent graft to occur in zones 0 or 1.
- Had a thoracic aneurysm with a contained rupture or localized at the anastomosis of a previous graft (pseudo-/false aneurysm).
- Had mycotic aneurysm.
- Had a dissection (type A or B) or an intramural hematoma or an aortic rupture in addition to the thoracic aneurysm.
- Required emergent aneurysm treatment, e.g., trauma or rupture.
- Received a previous stent or stent graft or previous surgical repair in the ascending and/or descending thoracic aorta, and/or in the aortic arch.
- Required surgical or endovascular treatment of an infra-renal aneurysm at the time of implant.
- Previous surgical or endovascular treatment of an infra-renal aortic aneurysm.
- Treatment with the Valiant Evo Thoracic Stent Graft System would require intentional revascularization of the brachio-cephalic artery or the left common carotid artery or the celiac trunk.
- Had planned to have a major surgical or interventional procedure within 30 days before or 30 days after the planned implantation of the Valiant Evo Thoracic Stent Graft System, exclusive of planned procedures that are needed for the safe and effective placement of the stent graft.
- Had a significant and/or circumferential aortic mural thrombus at either the proximal or distal attachment sites that could compromise fixation and seal of the implanted stent graft.
- Had a connective tissue disease.
- Had a bleeding diathesis or coagulopathy, or refused blood transfusion.
- Had a MI within 3 months of the procedure.
- Had a CVA within 3 months of the procedure.
- Had a known allergy or intolerance to the device materials
- Had a known allergy to anesthetic drugs

- Had a known hypersensitivity or contraindication to anticoagulants, or contrast media, which is not amenable to pretreatment.
- Had an active or systemic infection at the time of the index procedure.

2. Follow-up Schedule

All subjects in the study were scheduled to return for follow-up examinations at 1 month and 12 months postoperatively, and all subjects in the US sites were scheduled for an additional follow-up examination within 6 months postoperatively. Further follow-up evaluations are scheduled for all subjects who signed an updated Informed Consent Form for follow-up at 24 months, 36 months, 48 months, and 60 months, postoperatively. Forty one (41) of 100 subjects (37 of the 87 enrolled at the database lock for this PMA-S) signed the updated Informed Consent Form for 5 year follow-up, and reconsent is pending for 21 of 100 subjects (15 of the 87 at the database lock for this PMA-S). Thirty eight (38) of 100 subjects (35 of the 87 enrolled at the database lock for this PMA-S) are not participating in the 5 year follow-up and will participate in the study until the completion of their 2 year follow-up, as originally required.

Preoperatively, subjects underwent a comprehensive medical evaluation, American Society of Anesthesiologists (ASA) classification, appropriate imaging, and an assessment of the indication for Thoracic Endovascular Aortic Repair (TEVAR), as shown in **Table 5**. Postoperatively, the objective parameters measured during the study included the number of devices implanted, the configuration of each type of Valiant Evo Thoracic Stent Graft System implanted at the index procedure, implant zone of the most proximal component, adjunctive procedure, left subclavian artery (LSA) coverage information as the Valiant Evo stent graft can be landed in zone 2 thereby covering the ostium of the LSA either fully or partially, acute procedure observations and clinical utility measures and the effectiveness measures shown in the tables below. Adverse events and complications will be recorded at all visits.

Table 5: Data Collection Schedule

DATA	Screening /Baseline	Index Procedure	Hospital Discharge	1-Mo. F/U (±15 days)	6-Mo. F/U[d] (±30 days)	12-Mo. F/U (±60 days)
GENERAL						
Informed Consent	✓					
Inclusion Criteria/ Exclusion Criteria	✓					
Physical Examination	✓			✓	✓	✓
Medical History	✓					
Current Health Status and Risk Factors	✓					

DATA	Screening /Baseline	Index Procedure	Hospital Discharge	1-Mo. F/U (±15 days)	6-Mo. F/U[d] (±30 days)	12-Mo. F/U (±60 days)
Device and Procedure Information		✓				
Pre-implant Adjunctive Procedures		✓				
Hospital Discharge Information			✓			
Adverse event assessment	✓[a]	✓	✓	✓	✓	✓
EQ-5D questionnaire	✓			✓	✓	✓
IMAGING						
CT/MRI with contrast [b]	✓[g]			✓[c,e,g]	✓[e,g]	✓[e,h]
Angiography		✓[f]				

[a] In case of screen failures, investigators will be requested to enter safety information in the electronic case report form (eCRF) from time point of enrollment until time point of screen failure
[b] CT evaluation may include "3-phase technique", volume studies, 3-D reconstruction, or computer-aided measurements
[c] A CT/MRI with contrast acquired at discharge (or before Day 15) due to medical necessity may be used to meet the 1-month follow-up visit CT/MRI requirement if a CT/MRI with contrast cannot be obtained within the 1-month follow-up window due to the subject's health status based upon physician discretion.
[d] For subjects enrolled in the Valiant Evo International Clinical Trial in European countries, a six month follow up visit is not required per protocol.
[e] MRI with contrast may be used for those patients experiencing renal failure or who are otherwise unable to undergo contrast-enhanced CT scan, with Transesophageal echocardiography (TEE) being an additional option in the event of suboptimal MR imaging.
[f] Required to complete Procedure eCRF but not expected to be submitted to Medtronic or Core Lab unless further analysis is needed.
[g] Imaging assessed by core lab.
[h] Upon sponsor request, core lab analysis of imaging may be required.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to safety and effectiveness, the primary endpoint for the global cohort is a composite endpoint of both. It is defined as the proportion of subjects with access failures, deployment failures, and/or Major Device Effects (MDE) within 30 days post index procedure. For this study, access failure is defined as the inability to insert the device due to mechanical failure or anatomic exclusions of the femoral or iliac arteries. Deployment failure is defined as failure of deployment due to subject anatomy or mechanical failure. MDEs are defined as the occurrence of any of the following: device-related secondary procedures, device-related mortality,

conversion to open surgery, and thoracic aortic aneurysm rupture.

This primary endpoint was selected based on Medtronic's review of the design characteristics/components that were leveraged from Valiant Captivia Thoracic Stent Graft System to Valiant Evo Thoracic Stent Graft System. This review suggested that the design changes should only potentially impact device delivery and acute clinical outcomes, not long-term device performance. Access and deployment failures with the components of MDE comprise a clinically relevant measure of the effects of the design modifications because this composite endpoint addresses the potential failures relevant to the modifications. In addition, as MDEs are influenced little by aortic pathology, these measures are representative of device performance and are relatively independent of lesion type. Finally, results of the VALOR II (IDE study for Valiant Captivia Thoracic Stent Graft System in aneurysm conditions) clinical data showed that predominance of the MDEs occur within 30-days. As a result, the Valiant Evo IDE endpoint includes access failures, deployment failures, and MDEs at 30 days that were defined to include the potential clinical impacts that are related to the acute safety and effectiveness of stent graft placement.

Notably, the definition of deployment failure used for this study does not include deployment accuracy, deployment without the need for the use of bailout techniques, or the need for placing unintended additional devices. As such, FDA requested an ad hoc analysis of the primary endpoint to include these events which would generally count as delivery and deployment failures in endovascular graft studies.

Secondary objectives of the study included descriptive analyses of secondary endpoints, acute procedural observations and clinical utility measures. Secondary endpoints included adverse events (major adverse events (MAEs) and serious adverse events (SAEs)), MDEs, secondary procedures, all-cause mortality (ACM), aneurysm-related mortality (ARM), loss of stent graft patency, endoleaks, stent graft migration and aneurysm expansion.

With regards to study success/failure criteria, the study would be considered successful if the performance goal for the composite safety/effectiveness primary endpoint was met.

B. Accountability of PMA-S Cohort

A total of 49 subjects failed screening after consent. The reasons for exclusion included subject anatomy did not meet criteria (n=22), investigator withdrew consent prior to procedure (n=8), previous aortic repair (n=4), DTAA not between LSA and celiac trunk (n=3), significant or circumferential aortic mural thrombus (n=3), previous repair of an infra-renal aortic aneurysm (n=3), inadequate arterial access site (n=2), life expectancy of less than 1 year (n=2), dissection, intramural

hematoma, or aortic rupture (n=2), subject withdrew consent (n=2), major surgical intervention planned within 30 days (n=1), subject died prior to implant (n=1). Subject may have more than 1 reason for screen failure, thus, the total number rejected may be greater than the number of subjects that were screen failures.

At the time of database lock, 87 of the 100 subjects had been enrolled in the PMA study. The analysis for the study was based on these first 87 subjects evaluable for the 30-day endpoint. As shown in **Table 6** below, all 87 subjects were implanted with the Valiant Evo Thoracic Stent Graft System, and one subject died between implant and the 1-month visit window. Thus, a total of 86 subjects were available for the 1-month follow-up visit, with 84 (98%) of these having imaging follow-up. A total of 36 subjects completed the 6-month clinical and imaging follow-up, although this was not required of the OUS subjects. A total of 24 subjects were eligible for the 12-month clinical follow-up, with 21 of these (88%) having imaging follow-up.

Table 6: Subject and Core Lab Imaging Accountability – All Subjects[1]

	Subject Follow-up			**Subjects with Imaging (Core Lab)**		**Subjects with Adequate Imaging to Assess the Parameter (Core Lab)**				**Subject Events Occurring before Next Visit**					
Follow-up (Interval)	Eligible	Clinical Follow-up	Imaging Follow-up	CT \MR Imaging	Other Imaging[2]	Loss of Patency	Endoleak	Migration	Aneurysm Expansion	No Implant	Conversion to Surgery	Death	Withdrawal/Early Termination	Lost to Follow-up	Not Due for Next Visit
Enrollment	87									0					
Events after Implant but before 1-Month Visit											0	1	0	0	0
1-Month Visit (Day 1-90)	86	85 (99%)	84 (98%)	84 (98%)	0 (0.0%)	81 (94%)	81 (94%)								
Events after 1- Month but before 6- Month Visit											0	4	2	0	29
6-Month Visit (Day 91-304)[3]	51	36 (71%)	36 (71%)	36 (71%)	0 (0.0%)	31 (61%)	31 (61%)	35 (69%)	36 (71%)						
Events after 6- Month but before 12- Month Visit											0	1	0	0	26

Follow-up (Interval)	Subject Follow-up			Subjects with Imaging (Core Lab)		Subjects with Adequate Imaging to Assess the Parameter (Core Lab)				Subject Events Occurring before Next Visit					
	Eligible	Clinical Follow-up	Imaging Follow-up	CT \MR Imaging	Other Imaging[2]	Loss of Patency	Endoleak	Migration	Aneurysm Expansion	No Implant	Conversion to Surgery	Death	Withdrawal/Early Termination	Lost to Follow-up	Not Due for Next Visit
12-Month Visit (Day 305-548)	24	22 (92%)	21 (88%)	21 (88%)	0 (0.0%)	21 (88%)	21 (88%)	21 (88%)	21 (88%)						

[1] Data analysis sample size varies for each of the timepoints above. This variability is due to subject availability for follow-up, as well as, quantity and quality of images available from specific timepoints for evaluation. For example, the number of quality images available for evaluation of endoleak at 1 months is different than the number and quality of images available at 6 months due to variation in the number of images performed, the number of images provided from the clinical site to the Core Lab, and/or the number of images with acceptable evaluation quality.
[2] Other imaging includes chest X-ray, angiogram, ultrasound, and other imaging of the stent graft region.
[3] 6-month data is not required per OUS protocol; therefore, the follow-up rate is lower when US and OUS results are combined at this timepoint.

C. Study Population Demographics and Baseline Parameters

Demographics

The demographics of the global study population are typical for a descending thoracic aortic aneurysm study performed in the US and are summarized in **Table 7** below**.** The median age of the global cohort was 72.0 years (ranging from 51 to 89 years) and was similar between the US and OUS cohorts and between genders. Of the 87 subjects enrolled in the global cohort, a total of 37.9% (33/87) were female; the gender distribution in the US cohort was 50.0% female (26/52), with the OUS cohort having a lower proportion of females (20.0%, 7/35 subjects). Racial data was only collected among the US cohort, with 78.8% (41/52) of the US subjects reported as white. Other baseline characteristics are covered in the preoperative **Table 8** through **Table 11**.

Table 7: Subject Demographics

Subject Characteristics	Statistics/Category	Global Cohort
Gender		
	Female	37.9% (33/87)
	Male	62.1% (54/87)
Age (years)		
Total Population	n	87
	Mean ± SD	70.8 ± 8.7
	Median	72.0

Subject Characteristics	Statistics/Category	Global Cohort
	Min, max	51, 89
Female	n	33
	Mean ± SD	71.0 ± 8.7
	Median	73.0
	Min, max	51, 83
Male	n	54
	Mean ± SD	70.7 ± 8.7
	Median	72.0
	Min, max	54, 89
Race[1]		
	White	78.8% (41/52)
	Non-white	21.2% (11/52)
[1]Race data were not collected in OUS per regulation.		

Medical History

Baseline medical history characteristics from the global cohort are summarized in **Table 8**. The most prevalent cardiovascular medical history diagnoses at baseline included:

- Hypertension in 89.7% (78/87) of subjects
- Hyperlipidemia in 73.3% (63/86) of subjects
- Tobacco use in the last 10 years in 51.2% (44/86) of subjects

Overall, the US cohort presented with higher rates of comorbidities at baseline, compared to the OUS cohort, indicating the US subjects were less healthy than OUS subjects. This trend is confirmed in **Table 9**, which discusses the classifications of the majority of US subjects as Class III and Class IV based on the American Society of Anesthesiologists (ASA) Physical Status Classification System, compared to OUS subjects as Class II or Class III.

Table 8: Medical History

Body System / Condition	US (N=52)	OUS (N=35)	Global Cohort (N=87)
Alcoholism	9.6% (5/52)	2.9% (1/35)	6.9% (6/87)
Cancer	32.7% (17/52)	11.4% (4/35)	24.1% (21/87)
Carotid Artery Disease	28.8% (15/52)	6.3% (2/32)	20.2% (17/84)
Diabetes	25.0% (13/52)	14.3% (5/35)	20.7% (18/87)
Hyperlipidemia	78.8% (41/52)	64.7% (22/34)	73.3% (63/86)
Hypertension	94.2% (49/52)	82.9% (29/35)	89.7% (78/87)
Tobacco Use in the Last 10 Years	54.9% (28/51)	45.7% (16/35)	51.2% (44/86)

Body System / Condition	US (N=52)	OUS (N=35)	Global Cohort (N=87)
Cardiac Disease			
Angina	9.6% (5/52)	11.4% (4/35)	10.3% (9/87)
Arrhythmia	36.5% (19/52)	14.3% (5/35)	27.6% (24/87)
Congestive Heart Failure	19.2% (10/52)	2.9% (1/35)	12.6% (11/87)
Coronary Artery Disease	42.3% (22/52)	25.7% (9/35)	35.6% (31/87)
Coronary Artery Bypass Graft (CABG)	31.8% (7/22)	22.2% (2/9)	29.0% (9/31)
Percutaneous Coronary Intervention	54.5% (12/22)	77.8% (7/9)	61.3% (19/31)
Myocardial Infraction (MI)	13.5% (7/52)	20.0% (7/35)	16.1% (14/87)
Valvular Heart Disease (VHD)	11.5% (6/52)	8.6% (3/35)	10.3% (9/87)
Cardiac Valve Replacement or Repair	16.7% (1/6)	33.3% (1/3)	22.2% (2/9)
Pulmonary			
Chronic Obstructive Pulmonary Disease (COPD)	40.4% (21/52)	20.6% (7/34)	32.6% (28/86)
Renal			
Renal Insufficiency	26.9% (14/52)	14.3% (5/35)	21.8% (19/87)
Renal Failure	11.5% (6/52)	2.9% (1/35)	8.0% (7/87)
Cerebrovascular/Neurological			
Stroke/Cerebral Vascular Accident (CVA)	9.6% (5/52)	8.6% (3/35)	9.2% (8/87)
Transient Ischemic Attack (TIA)	11.5% (6/52)	2.9% (1/35)	8.0% (7/87)
Paraparesis	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)
Paraplegia	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)
Vascular			
Abdominal Aortic Aneurysm	21.2% (11/52)	31.4% (11/35)	25.3% (22/87)
Ascending Thoracic Aneurysm	17.3% (9/52)	2.9% (1/35)	11.5% (10/87)
Descending Thoracic Aneurysm	100.0% (52/52)	100.0% (35/35)	100.0% (87/87)
Family History of Aneurysm	12.5% (6/48)	12.5% (4/32)	12.5% (10/80)
Peripheral Vascular Disease	21.2% (11/52)	8.8% (3/34)	16.3% (14/86)
Connective Tissue Disease			
Marfan Syndrome	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)
Ehlers Danlos	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)
Other Systemic Conditions			
Bleeding Disorder	1.9% (1/52)	0.0% (0/35)	1.1% (1/87)
GI conditions	46.2% (24/52)	20.0% (7/35)	35.6% (31/87)

Body System / Condition	US (N=52)	OUS (N=35)	Global Cohort (N=87)
Liver Disease	7.7% (4/52)	0.0% (0/35)	4.6% (4/87)
Other Relevant Systemic Condition	65.4% (34/52)	40.0% (14/35)	55.2% (48/87)
Note: The subjects checked "unknown" or left blank for a certain question will not be included in the denominator.			
Other: Other relevant systemic conditions in 55.2% (48/87) of subjects, which includes, but is not limited to: chronic kidney disease, vocal cord paralysis, sleep apnea, gall stones, anxiety, cataracts, gout, and varicose veins			

ASA Classification

Based on their medical history and physical condition, all subjects were classified into five distinct categories according to the ASA Physical Status Classification System. The purpose of this grading system was to assess the physical status of the subject prior to the implant procedure.

The ASA Physical Status Classification on the 87 subjects enrolled in the global cohort is described in **Table 9**. The majority (44.8%, 39/87) of all subjects were Class III; the majority (90.4%, 47/52) of US subjects were Class III or Class IV; the majority (77.1%, 27/35) of OUS subjects were Class II or Class III.

Table 9: The American Society of Anesthesiologists (ASA) Physical Status Classification

ASA Physical Status Classification	US	OUS	Global Cohort
I (Normal healthy subject)	0.0% (0/52)	17.1% (6/35)	6.9% (6/87)
II (Subject with mild systemic disease)	9.6% (5/52)	40.0% (14/35)	21.8% (19/87)
III (Subject with severe systemic disease)	50.0% (26/52)	37.1% (13/35)	44.8% (39/87)
IV (Subject with severe systemic disease that is a constant threat to life)	40.4% (21/52)	5.7% (2/35)	26.4% (23/87)
V (Moribund subject who is not expected to survive without the operation)	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)
Not Assessed	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)

Baseline Vessel Measurements

Table 10, **Table 11**, and **Table 12** display the baseline vessel diameter and length measurements obtained by the core lab.

Table 10 summarizes the core lab reported pre-implant vessel diameters.The mean maximum aneurysm diameter of the global cohort reported by the core lab was 55.7 ± 13.1 mm, and the majority of subjects (40.2%; 35/87) had a maximum aneurysm diameter between 50 to 60 mm. The US and OUS cohorts had similar reported access vessel and aortic diameter measures.

Table 10: Pre-Implant Vessel Diameters, in mm, as Reported by Core Lab

Vessel Diameters (mm)	Statistics	Global Cohort
D1: Aorta Diameter (2 cm proximal to aneurysm)	n[1]	87
	Mean ± SD	29.3 ± 3.6
	Median	29.2
	Min, Max	20, 37
D2: Aorta Diameter (immediately proximal to the aneurysm)	n[1]	87
	Mean ± SD	31.6 ± 5.0
	Median	31.5
	Min, Max	20, 45
D3: Maximum Aneurysm Diameter	n[1]	87
	Mean ± SD	55.7 ± 13.1
	Median	55.4
	Min, Max	26, 98
	<30	1.1% (1/87)
	30 – <40	12.6% (11/87)
	40 – <50	13.8% (12/87)
	50 – <60	40.2% (35/87)
	60 – <70	23.0% (20/87)
	70 – <80	4.6% (4/87)
	80 – <90	2.3% (2/87)
	90 – <100	2.3% (2/87)
	≥ 100	0.0% (0/87)
D4: Aorta Diameter (immediately distal to the aneurysm)	n[1]	87
	Mean ± SD	30.4 ± 5.4
	Median	30.4
	Min, Max	19, 42
D5: Aorta Diameter (2 cm distal to the aneurysm)	n[1]	87
	Mean ± SD	29.2 ± 4.7
	Median	28.6
	Min, Max	20, 40
D6: Minimum Left Common Iliac Diameter	n[1]	86
	Mean ± SD	9.7 ± 2.5

Vessel Diameters (mm)	Statistics	Global Cohort
	Median	9.7
	Min, Max	5, 18
D7: Minimum Left External Iliac Diameter	n[1]	85
	Mean ± SD	7.7 ± 1.9
	Median	7.4
	Min, Max	4, 12
D8: Minimum Left Femoral Diameter	n[1]	83
	Mean ± SD	7.8 ± 1.7
	Median	7.7
	Min, Max	5, 12
D9: Minimum Right Common Iliac Diameter	n[1]	86
	Mean ± SD	9.8 ± 2.5
	Median	9.5
	Min, Max	5, 18
D10: Minimum Right External Iliac Diameter	n[1]	85
	Mean ± SD	7.5 ± 1.8
	Median	7.2
	Min, Max	3, 12
D11: Minimum Right Femoral Diameter	n[1]	83
	Mean ± SD	7.7 ± 1.6
	Median	7.5
	Min, Max	5, 11
Aorta Diameter at Left Subclavian Artery	n[1]	87
	Mean ± SD	29.8 ± 4.2
	Median	29.0
	Min, Max	23, 43
Aorta Diameter 2 cm Distal to Left Common Carotid Artery	n[1]	87
	Mean ± SD	29.7 ± 4.1
	Median	29.3
	Min, Max	22, 42
Aorta Diameter 2.5 cm Distal to Left Common Carotid Artery	n[1]	87
	Mean ± SD	30.3 ± 4.8
	Median	29.6

Vessel Diameters (mm)	Statistics	Global Cohort
	Min, Max	21, 42
Aorta Diameter 2.5 cm Proximal to Aneurysm	n[1]	87
	Mean ± SD	29.6 ± 3.5
	Median	29.6
	Min, Max	20, 38
Aorta Diameter 2 cm Proximal to Celiac Artery	n[1]	87
	Mean ± SD	28.9 ± 5.5
	Median	27.9
	Min, Max	19, 43
Maximum Infrarenal Aortic Diameter	n[1]	87
	Mean ± SD	26.4 ± 7.3
	Median	25.8
	Min, Max	15, 48
[1]n =number of enrolled subjects with readable scans.		

Table 11 summarizes the core lab reported pre-implant vessel lengths. Core lab reported aneurysm lengths were longer among the US cohort (122.6 ± 70.3 mm) as compared to the OUS cohort (99.1 ± 72.1 mm). Distal neck lengths in OUS subjects (121.5 ± 71.5 mm) were longer than those in US subjects (83.8 ± 63.4 mm). US subjects had slightly longer proximal neck lengths (65.6 ± 51.2 mm) compared to OUS subjects (48.8 ± 28.4 mm).

Table 11: Pre-Implant Vessel Length, as Reported by Core Lab

Vessel Lengths (mm)	Statistics	Global Cohort
Proximal Neck Length	n[1]	87
	Mean ± SD	58.9 ± 44.1
	Median	40.8
	Min, Max	20, 210
L1: Length between Distal Edge of LCCA and Start of Aneurysm (centerline)	n[1]	87
	Mean ± SD	75.1 ± 50.8
	Median	54.7
	Min, Max	20, 216
L2: Length between Distal Edge of LSA and Start of Aneurysm (centerline)	n[1]	87

Vessel Lengths (mm)	Statistics	Global Cohort
	Mean ± SD	56.3 ± 50.2
	Median	38.1
	Min, Max	-15, 197
L3: Aneurysm Length (centerline, D2 to D4)	n[1]	87
	Mean ± SD	113.1 ± 71.5
	Median	109.0
	Min, Max	15, 262
L4: Distal Neck Length (non-aneurysmal neck to celiac axis)	n[1]	87
	Mean ± SD	99.0 ± 68.9
	Median	79.3
	Min, Max	20, 296

[1]n =number of enrolled subjects with readable scans.

Table 12 summarizes the core lab reported pre-implant vessel assessment for access and implant. Notably, similar rates of severe, moderate, and mild access artery tortuosity were reported between the US and OUS cohorts.

The US and OUS cohorts had similar rates of proximal neck and thoracic aorta tortuosity. Globally, a total of 84.9% (73/86) of subjects were reported as having mild abdominal aorta tortuosity, with similar rates of abdominal aorta tortuosity reported in both the US and OUS cohorts.

Table 12: Pre-Implant Vessel Assessment for Access and Implant as Assessed by Core Lab

Vessel Assessment (mm)	Statistics	Global Cohort
Access Artery Tortuosity	None	0.0% (0/86)
	Mild	10.5% (9/86)
	Moderate	18.6% (16/86)
	Severe	70.9% (61/86)
Access Artery Calcification	None	8.1% (7/86)
	Mild	54.7% (47/86)
	Moderate	33.7% (29/86)
	Severe	3.5% (3/86)
Proximal Neck Tortuosity	None	0.0% (0/87)
	Mild	74.7% (65/87)
	Moderate	9.2% (8/87)
	Severe	16.1% (14/87)

Vessel Assessment (mm)	Statistics	Global Cohort
Abdominal Aorta Tortuosity	None	0.0% (0/86)
	Mild	84.9% (73/86)
	Moderate	9.3% (8/86)
	Severe	5.8% (5/86)
Thoracic Aorta Tortuosity	Low	14.3% (11/77)
	High	85.7% (66/77)
Thrombus Presented in the Intended Landing Zone	No	83.7% (72/86)
	Yes	16.3% (14/86)
	Insignificant	15.1% (13/86)
	Significant	1.2% (1/86)
	Circumferential	0.0% (0/86)
Calcium Presented in the Intended Landing Zone	No	37.9% (33/87)
	Yes	62.1% (54/87)
	Insignificant	60.9% (53/87)
	Significant	1.1% (1/87)
	Circumferential	0.0% (0/87)

Primary TEVAR Indication

The Valiant Evo stent graft was used to treat fusiform aneurysms, saccular aneurysms and penetrating atherosclerotic ulcers in the Valiant Evo IDE study. The most common pathology treated by the Valiant Evo Thoracic Stent Graft System in the global cohort was fusiform aneurysm (42.5%; 37/87), followed by saccular aneurysm (36.8%; 32/87), as displayed in **Table 13** below.

The US cohort was most commonly treated for fusiform aneurysms (46.2%; 24/52), and the OUS cohort was treated equally for fusiform (37.1%; 13/35) and saccular aneurysms (37.1%; 13/35). Approximately one-fifth of the overall cohort was treated for a penetrating atherosclerotic ulcer (PAU).

Table 13: Primary Indication for Thoracic Endovascular Aortic Repair (TEVAR)

Primary Indication for TEVAR	US	OUS	Global Cohort
Fusiform Aneurysm	46.2% (24/52)	37.1% (13/35)	42.5% (37/87)
Saccular Aneurysm	36.5% (19/52)	37.1% (13/35)	36.8% (32/87)
Penetrating Atherosclerotic Ulcer	17.3% (9/52)	25.7% (9/35)	20.7% (18/87)

Number of Devices Implanted at Index Procedure

The total number of devices implanted at the index procedure are presented in **Table 14**. Since multiple stent graft configurations may be used per subject, the number of devices implanted exceeds the number of subjects enrolled. The majority of subjects (56.3%; 49/87) had 1 device implanted, and the mean number of devices used was 1.5 per subject. In the US cohort, the majority of subjects (88.5%; 46/52) had 1 or 2 devices implanted. No subjects in the OUS cohort had more than 2 devices implanted.

Table 44: Total Number of Devices Implanted at Index Procedure

Devices Implanted per Subject	Global Cohort
Mean ± SD	1.5 ± 0.7
Median	1.0
Min, Max	1, 4
1	56.3% (49/87)
2	36.8% (32/87)
3	4.6% (4/87)
4	2.3% (2/87)
≥ 5	0.0% (0/87)

Device Configurations at Index Procedure

The distribution of devices implanted as proximal pieces is presented in **Table 15**. The majority (74.7%; 65/87) of all subjects received a FreeFlo configuration as the proximal device, with 56.3% (49/87) of subjects receiving the FreeFlo Straight configuration. Proximal device configurations usage was similar in the US and OUS.

Table 55: Devices Implanted as Proximal Configuration at Index Procedure

Device Configuration	Global Cohort
FreeFlo	74.7% (65/87)
FreeFlo Straight	56.3% (49/87)
FreeFlo Tapered	18.4% (16/87)
Closed Web (CoveredSeal)	25.3% (22/87)
Closed Web Straight	21.8% (19/87)
Closed Web Tapered	3.4% (3/87)

Distal configurations implanted at the index procedure are displayed in **Table 16**. There were more distal devices implanted in US subjects (26) compared to OUS subjects (12).

Table 66: Devices Implanted as Distal Configuration at Index Procedure

Device Configuration	Global Cohort
FreeFlo	21.1% (8/38)

Device Configuration	Global Cohort
FreeFlo Straight	21.1% (8/38)
FreeFlo Tapered	0.0% (0/38)
Closed Web (CoveredSeal)	78.9% (30/38)
Closed Web Straight	60.5% (23/38)
Closed Web Tapered	18.4% (7/38)

Implant Zone of Proximal Component

The landing zones of the proximal component implanted in all subjects are presented in **Table 17**. Stratified by geography, proximal placement of the FreeFlo devices was most common in Zone 3 in the US (59.5%; 22/37), while Zone 4 was most common in OUS (35.7%; 10/28). Closed Web (CoveredSeal) devices were most commonly placed in Zone 4 in both the US (46.7%; 7/15) and OUS (57.1%; 4/7).

Table 17: Implant Zone of Proximal Component

Implantation Zone of Proximal Component	Global Cohort
FreeFlo	
Zone 1	0.0% (0/65)
Zone 2	30.8% (20/65)
Zone 3	47.7% (31/65)
Zone 4	21.5% (14/65)
Closed Web (Covered Seal)	
Zone 1	0.0% (0/22)
Zone 2	9.1% (2/22)
Zone 3	40.9% (9/22)
Zone 4	50.0% (11/22)

Procedural Data

Table 18 summarizes the acute procedural observations that were available at the time of implant for the 87 subjects analyzed.

In the US cohort, the mean duration of the procedure was 87.2 ± 44.2 minutes, which was comparable to the mean duration in the OUS cohort, 91.0 ± 65.5 minutes. In the US, 98.1% (51/52) of subjects underwent general anesthesia, while 85.7% (30/35) of OUS subjects underwent general anesthesia. The median hospital stay for the US cohort was similar to that of the OUS cohort, with 5.0 days and 4.0 days, respectively. In both the US and OUS, one subject had a prolonged hospital stay of over 30 days.

A few notable data points differed between the two cohorts. Access type varied between cohorts, with percutaneous access being the preferred method in the US (71.2%; 37/52), whereas surgical cut down was the preferred method OUS (80.0%;

28/35). Mean radiation exposure was twice as high in the US (1222.8 ± 1655.9 mGy) compared to OUS (521.3 ± 538.9 mGy). Additionally, more US subjects were admitted to the ICU after the index procedure (47/52) compared to the OUS cohort (16/35).

Table 78: Acute Procedure Observations and Clinical Utility Measures

Acute Procedural Data	Statistics/Category	Global Cohort
Duration of procedure (min)	n	87
	Mean ± SD	88.7 ± 53.4
	Median	72.0
	Min, Max	23, 281
Anesthesia Type % (m/n)	General	93.1% (81/87)
	Local	4.6% (4/87)
	Epidural	0.0% (0/87)
	Spinal	2.3% (2/87)
Access Type % (m/n)	Surgical cut down	49.4% (43/87)
	Percutaneous	50.6% (44/87)
Estimated Blood Loss (cc)	n	85
	Mean ± SD	94.0 ± 147.1
	Median	50.0
	Min, Max	0, 900
	<750 cc	98.8% (84/85)
	≥750 cc	1.2% (1/85)
Subjects Requiring Blood Transfusion	% (m/n)	2.3% (2/87)
Volume of Blood Transfused (cc)	n[1]	2
	Mean ± SD	600.0 ± 0.0
	Median	600.0
	Min, Max	600, 600
Volume of Contrast (mL)	n	87
	Mean ± SD	96.2 ± 52.8
	Median	80.0
	Min, Max	20, 300
Total Fluoroscopic Time (min)	n	87
	Mean ± SD	12.2 ± 8.8
	Median	10.0
	Min, Max	1, 53
Radiation Exposure (mGy)	n	68
	Mean ± SD	1016.5 ± 1452.5

Acute Procedural Data	Statistics/Category	Global Cohort
	Median	550.0
	Min, Max	31, 8502
Time in ICU after Index Procedure (hours)	n[2]	63
	Mean ± SD	67.4 ± 79.9
	Median	46.0
	Min, Max	14, 584
Days to Hospital Discharge	n	86
	Mean ± SD	7.1 ± 6.7
	Median	5.0
	Min, Max	1, 35

[1]Number of subjects who required blood transfusion.
[2]Number of subjects who had an ICU stay after index procedure.

Adjunctive Procedures

Table 19 shows adjunctive procedures performed preoperatively and intraoperatively. The distribution of subjects with complete, partial, or no coverage of the left subclavian artery (LSA) is summarized in **Table 20**. A total of 3 subjects in the global cohort had LSA coverage without a revascularization procedure, one with complete LSA coverage, and two with partial LSA coverage.

In the US cohort, the most common intraoperative adjunctive procedure was CSF drainage (23.1%; 12/52). The most frequent intraoperative adjunctive procedure in OUS subjects was usage of a balloon catheter (42.9%; 15/35).

Table 89: Adjunctive Procedures

	Global Cohort
Preoperative Adjunctive Procedures	
Left Subclavian Transposition	4.6% (4/87)
Left Carotid to Left Subclavian Bypass	12.6% (11/87)
Left Subclavian Embolization/Occlusion	4.6% (4/87)
Iliac Stenting	0.0% (0/87)
Other Adjunctive Procedures	6.9% (6/87)
Intraoperative Adjunctive Procedures	
Left Subclavian Transposition	3.4% (3/87)
Left Carotid to Left Subclavian Bypass	6.9% (6/87)
Left Subclavian Embolization/Occlusion	11.5% (10/87)
Embolization of Aneurysm Sac	0.0% (0/87)
Uncovered Aortic Stent	0.0% (0/87)
Iliac Stenting	4.6% (4/87)

	Global Cohort
Rapid Cardiac Pacing during Deployment	9.2% (8/87)
Balloon Catheter	29.9% (26/87)
CSF Drainage	17.2% (15/87)
Other Adjunctive Procedures	4.6% (4/87)

Table 20 shows the percentage of subjects that had complete, partial, or no coverage of the left subclavian artery (LSA). When coverage of the LSA by the Valiant Evo Thoracic Stent Graft System occurred, complete coverage of the LSA was the most common type of coverage, reported in 21.8% (19/87) of the global cohort. Partial coverage of the LSA by the Valiant Evo Thoracic Stent Graft System was reported in 3 subjects (3.4%; 3/87) in the global cohort. The US and OUS cohorts had similar rates of complete LSA coverage, while the US cohort had the only cases of partial LSA coverage and revascularization.

Table 20: LSA Coverage

LSA Coverage	Global Cohort
Complete	21.8% (19/87)
Subjects with revascularization procedure	20.7% (18/87)
Subjects without revascularization procedure	1.1% (1/87)
Partial	3.4% (3/87)
Subjects with revascularization procedure	1.1% (1/87)
Subjects without revascularization procedure	2.3% (2/87)
None	74.7% (65/87)

D. Safety and Effectiveness Results

As shown in **Table 21**, the primary composite endpoint was met and was statistically significant, with a p-value of < 0.0001. A total of 2.3% (2/87) subjects experienced the primary composite endpoint event within 30 days, with a 1-sided 97.5% upper confidence limit of 8.06%, lower than the performance goal of 16% (p-value <.0001). It signifies that this study met the pre-specified performance goal.

Table 21: Primary Endpoint

Primary Endpoint	Valiant Evo Thoracic Stent Graft System	1-sided 97.5% Upper Confidence Limit	Performance Goal	p-value[1]
Access Failures; Deployment Failures; and/or MDEs within 30 Days Post Index Procedure	2.3% (2/87)	8.06%	16%	<.0001

[1] p-value was based on a binomial distribution at the one-sided 0.025 statistical significance level.

Table 22 provides a breakdown of the primary composite endpoint analysis. MDEs consist of device-related secondary procedure, device related mortality, conversion to open surgery, or thoracic aneurysm rupture. No subjects were reported as having vessel access or deployment failures during the index procedure. A total of 2 (both OUS) subjects were reported having a total of 4 MDEs (each subject had 2 MDEs) within 30 days of the index procedure. One subject had a device-related secondary procedure and device-related mortality, both on day 1. A secondary procedure (open surgery) was performed in an attempt to treat a retrograde type A dissection. The secondary procedure (adjudicated as device-related) was not successful, and the subject died on day 1, with the mortality adjudicated as device-related. Another subject had a thoracic aortic aneurysm rupture and device-related secondary procedure (additional stent graft endovascular procedure), both on day 28. The secondary procedure (adjudicated as device-related) was performed to treat an aortic arch rupture caused by septicemia on day 5 following infection in a peripheral venous catheter. This subject died on day 35; the death occurred outside of the 30-day window, thus is not included in the primary endpoint.

The poolability on the primary endpoint between US and OUS data were assessed using Fisher's exact test and is shown in **Table 22**. A p-value of 0.159 suggested no statistically significant heterogeneity between US and OUS was observed in the primary endpoint.

Table 22: Primary Endpoint (Breakdown)

Breakdown of Primary Endpoint	US	OUS	Global Cohort	p-value[1]
Overall Event Rates within 30 Days[2]	0.0% (0/52)	5.7% (2/35)	2.3% (2/87)	0.159
Vessel Access Failure	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)	
Deployment Failure	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)	
Major Device Effects (MDE)	0.0% (0/52)	5.7% (2/35)	2.3% (2/87)	
Device-related Secondary Procedures [3]	0.0% (0/52)	5.7% (2/35)	2.3% (2/87)	

Breakdown of Primary Endpoint	US	OUS	Global Cohort	p-value[1]
Device-related Mortality [3]	0.0% (0/52)	2.9% (1/35)	1.1% (1/87)	
Conversion to Open Surgery	0.0% (0/52)	0.0% (0/35)	0.0% (0/87)	
Thoracic Aortic Aneurysm Rupture	0.0% (0/52)	2.9% (1/35)	1.1% (1/87)	

[1] Fisher's exact test for US and OUS data poolability.
[2] Overall event rates are defined as the event rate of access and/or deployment failures; and/or MDEs within 30 days post index procedure. A subject may experience multiple events; hence, number of subjects counted in the overall event rate or at upper level may not be the sum of those in each event at lower level.
[3] Relationship to device was adjudicated by the Clinical Event Committee (CEC).

Device Deficiencies

Although the primary endpoint for the study was focused on early success, including delivery and deployment, as noted above, the definition of the endpoint did not include deployment accuracy, deployment without the need for the use of bailout techniques, or the need for placing unintended additional devices. Some of these events were captured as 'device deficiencies.' These were reported by the sites and core lab, or identified by the sponsor as described below.

Site Reported Device Deficiencies

A total of 9.2% (8/87) of subjects were reported having at least one device deficiency from 0-30 days, all occurring at the time of implant, as shown in **Table 23**. Details on these device deficiencies are included below. The core lab did not review angiographic imaging from the procedure, and thus did not report any imaging observations and/or related device deficiencies related to the procedure. No device deficiencies were reported in any subject beyond 30 days by the investigational sites.

Table 23. Device Deficiencies (Site-Reported)

Device Deficiencies	0-30 Days	31-183 Days	184-365 Days
Any Device Deficiencies[a]	9.2% (8/87)	0.0% (0/36)	0.0% (0/21)
Any other failure/malfunction of Stent Graft, specify	1.1% (1/87)	0.0% (0/36)	0.0% (0/21)
Failure to release tip capture	2.3% (2/87)	0.0% (0/36)	0.0% (0/21)
Deployment Difficulty	4.6% (4/87)	0.0% (0/36)	0.0% (0/21)
Difficulty to remove delivery system	2.3% (2/87)	0.0% (0/36)	0.0% (0/21)

[a] Number of subjects who had one or more device deficiencies reported. A subject may have device deficiencies in more than one category; hence, number of subjects with any device deficiencies may not be the sum of those in each category. Each subject was only counted once in each category.

Note: In **Table 23**, denominator is number of subjects have reached the time period as indicated.

Failure to Release Tip Capture

A total of 2 (2.3%) subjects had reported device deficiencies related to a failure of the tip capture release. Both failures of the tip capture release were reported with the FreeFlo tapered configuration. In both cases, the physician employed the bailout

technique and disassembled the rear tip capture mechanism. The tip capture was released successfully, and the delivery system was removed without any further complications. No adverse events were reported due to these device deficiencies.

All implanting investigators were required to complete updated device training in order to understand the correct troubleshooting techniques needed to overcome tip capture release failure. Maneuvers include relieving the forward pressure in the delivery system by gently moving the guidewire and delivery system off the aortic wall. Refer to Section 10.8 of the Valiant Navion Thoracic Stent Graft System IFU for notes and cautions related to tip capture release.

Deployment Difficulty – Distal Device Movement

A total of 4 (4.6%) subjects had deployment difficulty, distal device movement, reported. Of the 4 deployment difficulties, 1 subject experienced distal device movement with 2 devices (FreeFlo straight configuration). Of the remaining 3 subjects, 1 distal device movement was reported with a FreeFlo straight configuration while the other two were reported with a FreeFlo tapered configuration. These subjects experienced distal device movement upon the deployment of the stent graft from the delivery system. Additional proximal devices were added in 2 subjects to ensure adequate proximal seal. No adverse events were reported related to these device deficiencies. All implanting investigators were required to complete updated device training in order to minimize the occurrence of distal device movement during device implant. Maneuvers to reduce the occurrence of distal device movement during deployment include rapid right ventricular pacing, controlled hypotension, and maintaining apposition of the delivery system and guidewire to the greater curve of the aorta. Refer to Section 10.8 of the Valiant Navion Thoracic Stent Graft System IFU for notes and instructions related to deploying the device.

Difficulty to Remove Delivery System

In a total of 2 (2.3%) subjects,difficulty to remove the delivery system was reported. One subject reported the difficulty to remove the delivery system with a FreeFlo straight configuration and the second subject with a FreeFlo tapered configuration. Both subjects had the tip capture fitting caught in a bare stent after the stent graft deployment and tip release. After manipulation of the delivery systems, the physicians were able to remove the device. One subject had no adverse events reported as associated with this device deficiency. One subject, who was considered a failure of the primary endpoint, had an adverse event (retrograde type A dissection) reported as related to this device deficiency, which resulted in the subject's death on day 1 (as reported in **Table 31**). A secondary procedure (open surgical repair) was performed to treat the retrograde type A dissection. The secondary procedure (adjudicated as device-related) was not successful, and the subject died on day 1, with the mortality adjudicated as device-related.

All implanting investigators were required to complete updated device training in order to understand the correct troubleshooting techniques needed to overcome difficulty removing the delivery system. Maneuvers include relieving the forward pressure in the delivery system before attempting to actuate the tip capture. Refer to Section 10.9 of the

Valiant Navion Thoracic Stent Graft System IFU for notes and cautions related to tip capture release.

Other Type of Stent Graft Malfunction

There was 1 (1.1%) reported case of an "other type of malfunction of the stent graft" in a subject. This was reported in a FreeFlo straight configuration. The physician reported that the Valiant Evo Thoracic Stent Graft System proximal device migrated 2 cm from the deployment landing zone during deployment of the distal stent graft extension during the index procedure. The distal stent graft extension was sized incorrectly for placement in an unsupported region of the aorta. The proximal seal zone was ballooned to prevent further distal movement, and no additional proximal extension was needed. The final angiogram showed no endoleaks, and no adverse events related to this event were reported. Refer to Section 10.8 of the Valiant Navion Thoracic Stent Graft System IFU for notes and instructions related to deploying the device.

Sponsor-Assessed Device Deficiencies:

There were 2 additional instances of distal device movement observed during the deployment process. The Sponsor assessed these distal device movements as device deficiencies, neither of which were assessed to have serious adverse device effect (SADE) potential. Neither subject was reported as having a clinical outcome related to these implant procedural observations.

Core Lab Reported Device Deficiencies:

Table 24 shows the core lab reported device deficiencies. The core lab reported device deficiencies were observed in a Closed Web (CoveredSeal) straight configuration. Misalignment of the distal stent ring was observed in 1 subject, where the distal most stent ring was not aligned perpendicular to the centerline of blood flow. Misalignment of distal stent ring was relative to the direction of the blood flow. This caused a stent peak on the distal most stent ring to be angled into the lumen. The investigator did not determine the imaging finding reported by the core lab to be a device deficiency. No adverse events were reported associated with this device deficiency.

Table 24. Core Lab Reported Device Deficiency

Subject #	Day of Follow-up Image	Device Deficiencies observed on the image	Comments
10309-001	43	Any other failure/malfunction of Stent Graft, specify:	Other Device Deficiency: Misalignment of distal stent ring relative to direction of blood flow.
10309-001	225	Any other failure/malfunction of Stent Graft, specify:	Other Device Deficiency: Misalignment of distal stent ring relative to direction of blood flow.

FDA requested a worst-case analysis (ad hoc analysis) for the primary endpoint including 4 additional events that would generally count against successful delivery and deployment, including inaccurate deployment, need for use of bailout procedures and unplanned implantation of additional devices. The worst-case analysis met the performance goal of the Valiant Evo Thoracic Stent Graft System IDE study and is provided in **Table 25** below.

Table 25: Primary Endpoint Worst-Case Analysis per FDA's Definition of Successful Delivery and Deployment

Primary Endpoint with Worst Case Analysis per FDA Definition of Successful Deployment			
Primary Endpoint	**Valiant Evo Thoracic Stent Graft System**	**1-sided 97.5% Upper Confidence Limit**	**Performance Goal**
Access Failures; Deployment Failures; and/or MDEs within 30 Days Post Index Procedure	6.9% (6/87)	14.41%	16%

To evaluate whether the steps taken to avoid additional device deficiencies in the study were effective, the timing of the events in relation to patient enrollment was considered and is presented in **Tables 26** and **27**. Although some of the events occurred later in the study, all but one happened prior to the implementation of the associated mitigation strategies.

After completion of the refresher training to mitigate deployment difficulties and any other failure/malfunction of stent graft, 77 remaining subjects of the Valiant Evo IDE study were enrolled. One additional event (subject 00003-001) related to deployment difficulty occurred after the refresher training. After the device deficiency occurred, the case was verbally discussed, and the content of the refresher training was reiterated. No additional deployment difficulties were reported after this event.

Post completion of the refresher training to mitigate failure to release tip capture and difficulty to remove delivery system, 30 and 15 subjects were enrolled, respectively.

Table 26: Site Reported Device Deficiencies

Subject ID	**Device Deficiency Type**	**Overall Subject Number Enrolled in Study (out of 87)**	**Overall Implant Order at Site**
00001-001	Any other failure/malfunction of Stent Graft	3	1 of 2
00152-001	Deployment Difficulty	7	1 of 9
00020-004	Deployment Difficulty	18	3 of 10
00020-001	Failure to release tip capture	19	4 of 10
00003-001	Deployment Difficulty	27	1 of 2
00020-006	Deployment Difficulty + Failure to release tip capture*	46	6 of 10
10309-002	Difficulty to remove delivery	66	2 of 2

Subject ID	Device Deficiency Type	Overall Subject Number Enrolled in Study (out of 87)	Overall Implant Order at Site
	system		
13046-004	Difficulty to remove delivery system	74	3 of 3
*This deployment difficulty was related to the severely tortuous anatomy.			

Table 27: Core Lab Reported Device Deficiencies

Subject ID	Device Deficiency Type	Overall Subject Number Enrolled in Study (out of 87)	Overall Implant Order at Site
10309-001	Any other failure/malfunction of Stent Graft: Misalignment of distal stent ring relative to the blood flow	39	1 of 2

1. Additional Safety Results

With regards to safety, secondary endpoints were collected as shown in **Table 28** below. The key safety outcomes for this study are presented in **Table 29** through **Table 31**.

Table 28: Secondary Endpoints (Excluding Imaging Findings)

Time Period **Secondary Endpoints**	**Global Cohort**
0 - 30 Days	
Peri-operative Mortality	2.3% (2/87)
All Adverse Events[1,2](AE)	73.6% (64/87)
Major Adverse Events (MAE)	28.7% (25/87)
Serious Adverse Events (SAE)	32.2% (28/87)
Secondary Procedures[2]	2.3% (2/87)
Secondary Endovascular Procedures	1.1% (1/87)
Secondary Surgical Procedure	1.1% (1/87)
0 - 183 Days	
All-cause Mortality	8.9% (5/56)
Aneurysm-related Mortality	5.5% (3/55)
Major Device Effects[2](MDE)	3.7% (2/54)
Device-related Secondary Procedures	3.7% (2/54)
Device-related Mortality	3.7% (2/54)
Conversion to Open Surgery	0.0% (0/52)
Thoracic Aortic Aneurysm Rupture	1.9% (1/53)

Time Period Secondary Endpoints	Global Cohort
All Adverse Events[1,2](AE)	92.1% (70/76)
Major Adverse Events (MAE)	40.8% (31/76)
Serious Adverse Events (SAE)	52.6% (40/76)
Secondary Procedures	5.6% (3/54)
Secondary Endovascular Procedures	3.8% (2/53)
Secondary Surgical Procedure	1.9% (1/53)
0 - 365 Days	
All-cause Mortality	17.6% (6/34)
Aneurysm-related Mortality	9.7% (3/31)
Major Device Effects[2](MDE)	9.7% (3/31)
Device-related Secondary Procedures	6.7% (2/30)
Device-related Mortality	9.7% (3/31)
Conversion to Open Surgery	0.0% (0/28)
Thoracic Aortic Aneurysm Rupture	3.4% (1/29)
All Adverse Events[1,2](AE)	93.3% (70/75)
Major Adverse Events (MAE)	45.3% (34/75)
Serious Adverse Events (SAE)	54.7% (41/75)
Secondary Procedures	9.7% (3/31)
Secondary Endovascular Procedures	6.7% (2/30)
Secondary Surgical Procedure	3.4% (1/29)

Note: Denominators included all enrolled subjects who either had an event within the time period or were followed for at least 1, 91, or 305 days for the time periods of 30, 183, and 365 days, respectively.
[1] All Adverse Events including, but not limited to, MAEs and SAEs.
[2] A subject may experience multiple events; hence, number of subjects counted in the overall event rate may not be the sum of those in each event.

Adverse effects that occurred in the IDE clinical study:

All-Cause Mortality

Table 29 and **Figure 3** show the Kaplan-Meier estimates of freedom from all-cause mortality through 365 days.

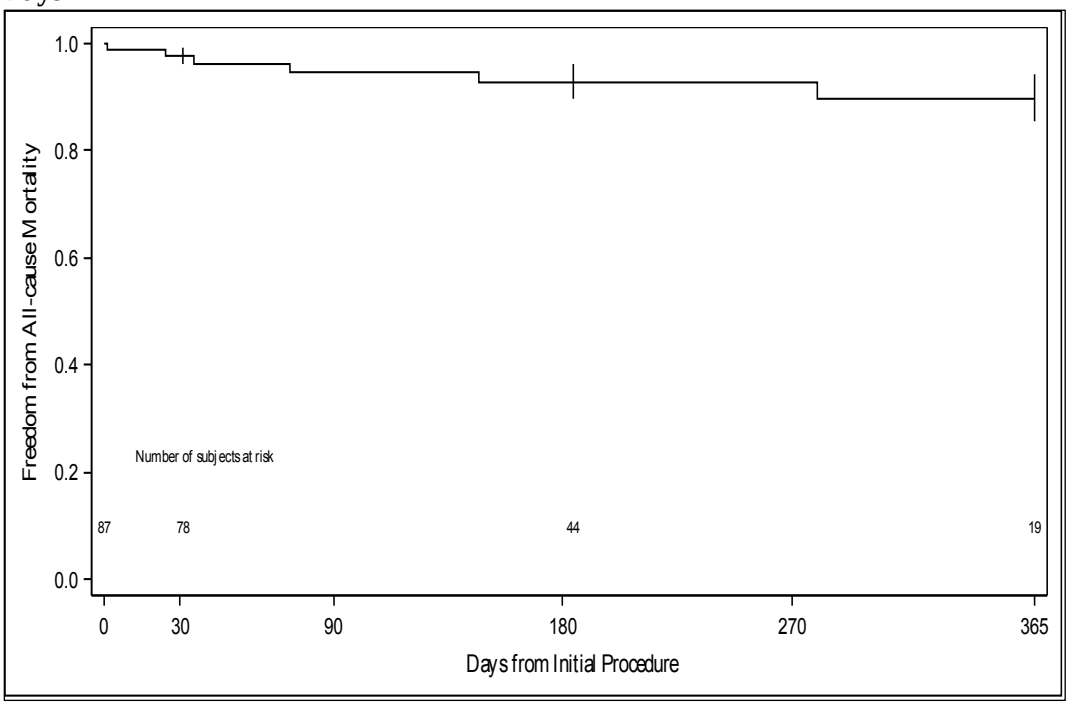
Table 29: Kaplan-Meier Estimates of Freedom from All-cause Mortality through 365 Days

All-cause Mortality	Treatment to 30 days	31 to 183 days	184 to 365 days
No. at Risk[1]	87	78	44
No. of Events	2	3	1
No. Censored[2]	7	31	24

All-cause Mortality	Treatment to 30 days	31 to 183 days	184 to 365 days
Kaplan-Meier Estimate[3]	0.977	0.928	0.898
Standard Error	0.016	0.032	0.043

[1]Number of subjects at risk at the beginning of interval.
[2]Subjects are censored because their last follow-up has not reached the end of the time interval or because they are lost to follow-up.
[3]Estimate made at end of time interval.

Figure 3: Kaplan-Meier Estimates of Freedom from All-cause Mortality through 365 Days



Aneurysm-Related Mortality

Aneurysm-related mortality (ARM), is defined as any death occurring within 30 days from either the initial procedure or any secondary procedure intended to treat the aneurysm, unless there is evidence to the contrary. Additionally, deaths occurring as a consequence of any procedure intended to treat the targeted aneurysm, aneurysm rupture, or a conversion to open repair are also considered as ARM. **Table 30** and **Figure 4** display the Kaplan-Meier estimate of ARM of the global cohort within 365 days of the index procedure. Freedom from ARM was reported in 97.7% of subjects from treatment to 30 days. The causes of ARM are presented in **Table 31**.

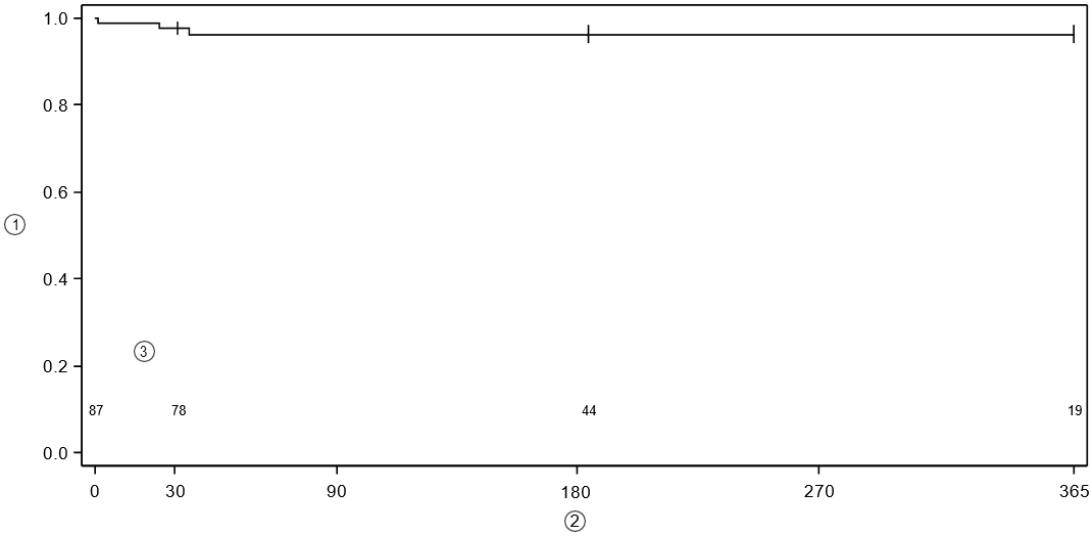
Table 90: Kaplan-Meier Estimates of Freedom from Aneurysm-related Mortality through 365 Days

Aneurysm-related Mortality	Treatment to 30 days	31 to 183 days	184 to 365 days
No. at Risk[1]	87	78	44

Aneurysm-related Mortality	Treatment to 30 days	31 to 183 days	184 to 365 days
No. of Events	2	1	0
No. Censored[2]	7	33	25
Kaplan-Meier Estimate[3]	0.977	0.964	0.964
Standard Error	0.016	0.021	0.021

[1]Number of subjects at risk at the beginning of interval.
[2]Subjects are censored because their last follow-up has not reached the end of the time interval or because they are lost to follow-up.
[3]Estimate made at end of time interval.

Figure 4: Kaplan-Meier Estimates of Freedom from Aneurysm-related Mortality through 365 Days



Deaths

Table 101 below summarizes the 6 deaths that occurred in the global cohort in this analysis. A total of 2 mortalities occurred within 30 days of the procedure, both aneurysm related. All deaths were adjudicated by the CEC who provided an independent evaluation based on their medical experience. A total of 3 deaths were adjudicated as aneurysm related (10309-002, 11080-002, 11081-001). The CEC adjudicated the death of subject 10309-002 as device and procedure related as it occurred within one day of the procedure. The CEC adjudicated the death of subject 11080-002 as procedure related as it occurred within 30 days. There was no evidence in the source documents provided to indicate device relatedness. The death of subject 11081-001 was due to an infection of the graft; if the subject did not have the graft implanted, nor the procedure, the infection possibly would not have occurred, thus the death was adjudicated as device and procedure related.

Please note that of the 6 deaths noted in **Table 31**, the retrograde Type A dissection in 10309-002 was caused by a device deficiency associated with removing the delivery system. All implanting investigators were required to complete updated device training in order to understand the correct troubleshooting techniques needed to overcome difficulty removing the delivery

system. Maneuvers include relieving the forward pressure in the delivery system before attempting to actuate the tip capture.

Table 101: Subject Deaths

			CEC Adjudication		
Subject #	**Adverse Events leading to Death**	**Day from Implant**	**Device Related**	**Procedure Related**	**Aneurysm Related**
10309-002	Retrograde dissection type A AORTA	1	Yes	Yes	Yes
11080-002	Death*	24	No	Yes	Yes
11081-001	Aortic arch rupture due to septicemia	35	Yes	Yes	Yes
00223-001	Tracheal Hemorrhage	73	No	No	No
00020-006	Worsening COPD	147	No	No	No
00078-001	Bacterial sepsis	280	Yes	Yes	No
*No death certificate was available; thus, the cause of death was unknown.					

Major Device Effects

MDEs are defined as the occurrence of any of the following: device-related secondary procedures, device-related mortality, conversion to open surgery, and thoracic aortic aneurysm rupture.

Table shows the major device effects adjudicated by the CEC through 365 days. Details of the breakdown of MDEs are displayed in **Table 32**. Of the 6 MDEs reported within 365 days, 50% (3/6) were device related mortalities, 33.3% (2/6) were device related secondary procedures, and 16.7% (1/6) was a TAA rupture. The 4 MDEs that occurred within 30 days were counted against the primary endpoint. Please see the primary endpoint analysis above for more details on these events. The device related mortality at 35 days was due to the DTAA rupture reported at 28 days and is also discussed in the primary endpoint analysis above. One US subject (00078-001) died of bacterial sepsis on Day 280 which was adjudicated as device related; the CEC acknowledged that the event appeared not to be related to the specific Valiant Evo Thoracic Stent Graft System, but rather is a known risk for any TEVAR procedure.

Table 32: CEC Adjudicated Major Device Effects (MDE) through 365 Days

Subject #	Days from Implant	CEC Term
10309-002	1	Device related mortality
10309-002	1	Device related secondary procedure
11081-001	28	DTAA Rupture
11081-001	28	Device related secondary procedure
11081-001	35	Device related mortality
00078-001	280	Device related mortality

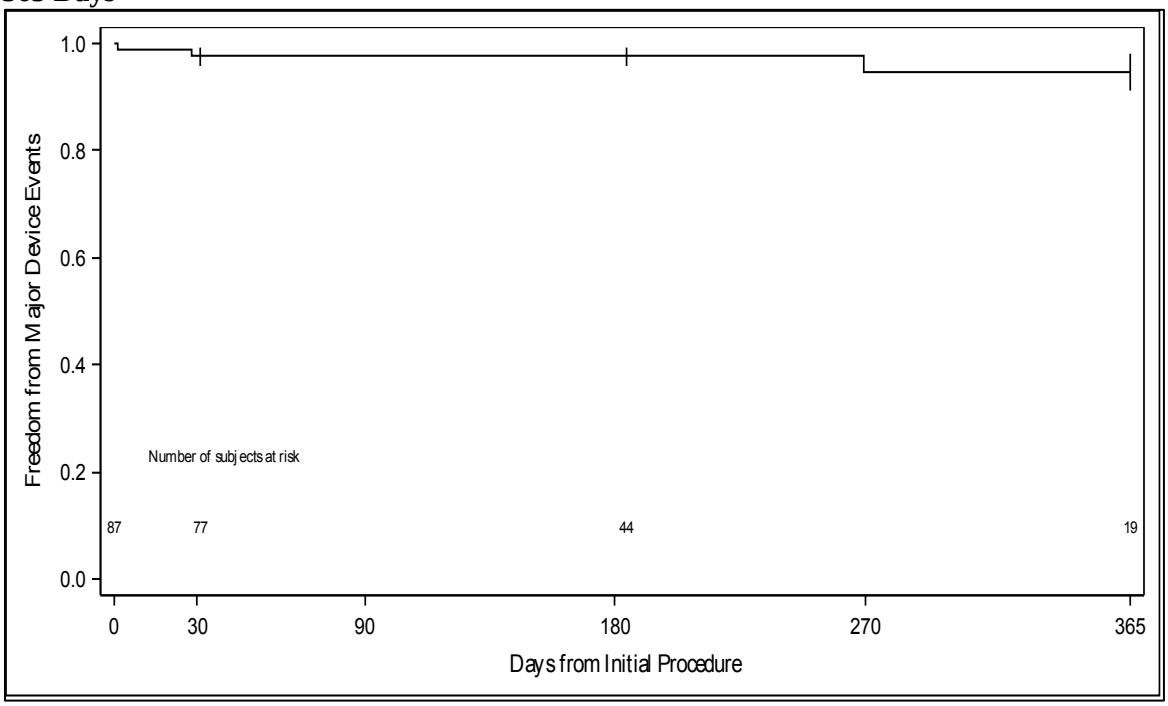
Table33 and **Figure 5** show Kaplan-Meier estimates of freedom from major device effects through 365 days.

Table 33: Kaplan-Meier Estimates of Freedom from Major Device Effects through 365 Days

Major Device Effects (MDE)	Treatment to 30 days	31 to 183 days	184 to 365 days
No. at Risk[1]	87	77	44
No. of Events	2	0	1
No. Censored[2]	8	33	24
Kaplan-Meier Estimate[3]	0.976	0.976	0.946
Standard Error	0.017	0.017	0.034

[1]Number of subjects at risk at the beginning of interval.
[2]Subjects are censored because their last follow-up has not reached the end of the time interval or because they are lost to follow-up.
[3]Estimate made at end of time interval.

Figure 5: Kaplan-Meier Estimates of Freedom from Major Device Effects through 365 Days



Major Adverse Events

Major adverse events (MAEs) are defined as the occurrence of any of the following:

- Respiratory complications: atelectasis/pneumonia, pulmonary embolism, pulmonary edema, respiratory failure
- Renal complications: renal failure, renal insufficiency

- Cardiac complications: Myocardial infarction (MI), unstable angina, new arrhythmia, exacerbation of congestive heart failure (CHF)
- Neurological complications: new cerebrovascular accident (CVA)/embolic events, paraplegia, paraparesis
- Gastrointestinal complications: bowel ischemia
- Major bleeding complication (procedural or post-procedural), coagulopathy
- Vascular complications: aortic rupture, aneurysm rupture, hematoma at access site, pseudo or false aneurysm, arteriovenous (AV) fistula, retroperitoneal bleed, limb ischemia, thrombosis.

Table 34 shows the MAEs reported under the IDE. The percentage of subjects who experienced one or more MAEs between 0-30 days was 28.7% (25/87) in the global cohort. The system organ class with the most MAEs was Cardiac Disorders (17.2%;15/87). The most frequent MAEs reported were atrial fibrillation (4.6%; 4/87) and acute renal failure (3.4%; 3/87). Of note, 2 subjects had aortic dissections reported between 0-30 days. One subject had a retrograde type A dissection on day 1 post index procedure, which was attempted to be repaired via an open surgical repair, and led to death on day 1. This event was counted against the primary endpoint. Please see the primary endpoint analysis above for more details. Another subject had a segmental aortic dissection at the distal neck on day 1. The subject experienced acute dorsal pain and a CT scan was performed which revealed a focal aortic dissection at the distal end of the stent graft. Invasive pressure monitoring was initiated along with medications. At the time of the data snapshot, the dissection was ongoing with the plan to continue monitoring and not to intervene.

The percentage of subjects who experienced one or more MAEs between 31-183 days was 10.3% (8/78) in the global cohort. The system organ class with the most MAEs was Cardiac Disorders (5.1%; 4/78). The most frequently reported MAE was atrial fibrillation (2.6%; 2/78). The percentage of subjects who experienced one or more MAEs between 184-365 days was 9.1% (4/44) in the global cohort. Cardiac Disorders was the most commonly reported category of MAE with 4.5% (2/44) of subjects.

Table 34: Major Adverse Events (MAE) (All Subjects, Site-Reported)

System Organ Class **Preferred Term**	**0-30 Days** **m[1] = 87**	**31-183 Days** **m[1] = 78**	**184-365 Days** **m[1] = 44**
Any Major Adverse Events (MAE[2])	**28.7% (25/87)**	**10.3% (8/78)**	**9.1% (4/44)**
Cardiac Disorders	17.2% (15/87)	5.1% (4/78)	4.5% (2/44)
Acute Myocardial Infarction	1.1% (1/87)	0.0% (0/78)	2.3% (1/44)
Angina Unstable	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Atrial Fibrillation	4.6% (4/87)	2.6% (2/78)	0.0% (0/44)
Atrial Tachycardia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Atrioventricular Block	1.1% (1/87)	0.0% (0/78)	2.3% (1/44)

System Organ Class Preferred Term	0-30 Days m[1] = 87	31-183 Days m[1] = 78	184-365 Days m[1] = 44
Atrioventricular Block First Degree	2.3% (2/87)	0.0% (0/78)	0.0% (0/44)
Bradycardia	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Cardiac Failure Acute	0.0% (0/87)	2.6% (2/78)	0.0% (0/44)
Cardiac Failure Congestive	2.3% (2/87)	1.3% (1/78)	2.3% (1/44)
Left Ventricular Failure	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Sinus Bradycardia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Sinus Tachycardia	2.3% (2/87)	1.3% (1/78)	0.0% (0/44)
Supraventricular Tachycardia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Tachycardia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Torsade De Pointes	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Ventricular Extrasystoles	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Ventricular Tachycardia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Infections and Infestations	0.0% (0/87)	1.3% (1/78)	2.3% (1/44)
Lung Infection	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Pneumonia	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Injury, Poisoning and Procedural Complications	2.3% (2/87)	1.3% (1/78)	0.0% (0/44)
Fat Embolism	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Procedural Haemorrhage	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Vascular Pseudoaneurysm	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Investigations	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Blood Creatinine Increased	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Nervous System Disorders	5.7% (5/87)	0.0% (0/78)	2.3% (1/44)
Cerebrovascular Accident	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Embolic Stroke	2.3% (2/87)	0.0% (0/78)	0.0% (0/44)
Ischaemic Stroke	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Paraplegia	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Spinal Cord Ischaemia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Renal and Urinary Disorders	3.4% (3/87)	0.0% (0/78)	2.3% (1/44)
Renal Failure Acute	3.4% (3/87)	0.0% (0/78)	2.3% (1/44)
Respiratory, Thoracic and Mediastinal Disorders	4.6% (4/87)	1.3% (1/78)	0.0% (0/44)
Acute Respiratory Failure	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Atelectasis	2.3% (2/87)	0.0% (0/78)	0.0% (0/44)
Pulmonary Congestion	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)

System Organ Class Preferred Term	0-30 Days m[1] = 87	31-183 Days m[1] = 78	184-365 Days m[1] = 44
Pulmonary Embolism	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Respiratory Distress	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Vascular Disorders	5.7% (5/87)	1.3% (1/78)	0.0% (0/44)
Aortic Dissection	2.3% (2/87)	0.0% (0/78)	0.0% (0/44)
Aortic Rupture	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Femoral Artery Occlusion	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Peripheral Artery Thrombosis	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Peripheral Ischaemia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)

[1]Number of subjects at risk at the beginning of the time interval and it is the denominator of event rate for the given time period.
[2]Percent (number) of subjects who experienced one or more Major Adverse Events (MAEs) during the time period. A subject may report multiple adverse events and in different categories; hence, number of subjects in each category may not be the sum of those in each subcategory. Each subject was only counted once in each category.

Serious Adverse Events

Serious adverse events (SAEs) are defined as adverse events that:

- led to death,
- led to serious deterioration in the health of the subject, that either resulted in
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function, or
  - in-patient or prolonged hospitalization, or
  - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
- led to fetal distress, fetal death or a congenital abnormality or birth defect.

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan (CIP), without serious deterioration in health, is not considered a serious adverse event.

Table 35 shows the SAEs reported under the IDE. The percentage of subjects who experienced one or more SAEs between 0-30 days was 32.2% (28/87) in the global cohort. The system organ class with the most SAEs was Cardiac Disorders (9.2%; 8/87), followed by Nervous System Disorders (8.0%; 7/87) and Vascular Disorders (8.0%; 7/87). The percentage of subjects who experienced one or more SAEs between 31-183 days was 24.4% (19/78) in the global cohort. The most frequently reported SAE were within the system organ classes of Respiratory, Thoracic and Mediastinal Disorders (6.4%; 5/78) and Vascular Disorders (6.4%; 5/78). The most commonly reported SAE was Chronic Obstructive Pulmonary Disease (3.8%; 3/78).The percentage of subjects who experienced one or more SAEs between 184-365 days was 22.7% (10/44) in the global cohort. Most SAEs reported were in

the system organ classes of Infections and Infestations (6.8%; 3/44) and Vascular Disorders (6.8%; 3/44).

Table 35: Major Adverse Events (MAE) (All Subjects, Site-Reported)

System Organ Class Preferred Term	0-30 Days m[1] = 87	31-183 Days m[1] = 78	184-365 Days m[1] = 44
Any serious AEs[2]	**32.2% (28/87)**	**24.4% (19/78)**	**22.7% (10/44)**
Blood and Lymphatic System Disorders	2.3% (2/87)	1.3% (1/78)	0.0% (0/44)
Anaemia	1.1% (1/87)	1.3% (1/78)	0.0% (0/44)
Anaemia Of Chronic Disease	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Neutrophilia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Cardiac Disorders	9.2% (8/87)	2.6% (2/78)	4.5% (2/44)
Acute Myocardial Infarction	1.1% (1/87)	0.0% (0/78)	2.3% (1/44)
Angina Unstable	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Atrial Fibrillation	3.4% (3/87)	1.3% (1/78)	0.0% (0/44)
Atrioventricular Block	1.1% (1/87)	0.0% (0/78)	2.3% (1/44)
Cardiac Failure Congestive	2.3% (2/87)	0.0% (0/78)	2.3% (1/44)
Left Ventricular Failure	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Tachycardia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Ventricular Tachycardia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Gastrointestinal Disorders	3.4% (3/87)	1.3% (1/78)	0.0% (0/44)
Colitis	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Faecal Incontinence	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Gastritis	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Gastrointestinal Haemorrhage	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Ileus	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Pancreatitis Acute	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
General Disorders and Administration Site Conditions	3.4% (3/87)	0.0% (0/78)	0.0% (0/44)
Death	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Pyrexia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Stent-Graft Endoleak	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Hepatobiliary Disorders	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Cholecystitis Acute	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Immune System Disorders	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Anaphylactic Shock	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Infections and Infestations	4.6% (4/87)	3.8% (3/78)	6.8% (3/44)
Bacterial Sepsis	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)

Device Related Infection	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Lung Infection	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Pneumonia	0.0% (0/87)	1.3% (1/78)	2.3% (1/44)
Sepsis	2.3% (2/87)	1.3% (1/78)	0.0% (0/44)
Urinary Tract Infection Bacterial	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Urinary Tract Infection Staphylococcal	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Urosepsis	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Injury, Poisoning and Procedural Complications	6.9% (6/87)	5.1% (4/78)	4.5% (2/44)
Cervical Vertebral Fracture	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Facial Bones Fracture	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Fat Embolism	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Hand Fracture	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Mental Status Changes Postoperative	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Overdose	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Post Lumbar Puncture Syndrome	2.3% (2/87)	0.0% (0/78)	0.0% (0/44)
Spinal Compression Fracture	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Tracheal Haemorrhage	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Vascular Pseudoaneurysm	1.1% (1/87)	1.3% (1/78)	0.0% (0/44)
Wound Dehiscence	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Investigations	1.1% (1/87)	1.3% (1/78)	0.0% (0/44)
Blood Creatinine Increased	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Weight Decreased	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Metabolism and Nutrition Disorders	2.3% (2/87)	1.3% (1/78)	2.3% (1/44)
Fluid Overload	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Hyponatraemia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Malnutrition	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Vitamin D Deficiency	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Musculoskeletal and Connective Tissue Disorders	1.1% (1/87)	2.6% (2/78)	2.3% (1/44)
Arthritis	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Muscular Weakness	1.1% (1/87)	1.3% (1/78)	0.0% (0/44)
Pain in Extremity	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Pseudarthrosis	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	0.0% (0/87)	2.6% (2/78)	0.0% (0/44)

Bladder Cancer Recurrent	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Squamous Cell Carcinoma	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Nervous System Disorders	8.0% (7/87)	1.3% (1/78)	4.5% (2/44)
Cerebrovascular Accident	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Dementia with Lewy Bodies	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Embolic Stroke	2.3% (2/87)	0.0% (0/78)	0.0% (0/44)
Hypoaesthesia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Ischaemic Stroke	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Metabolic Encephalopathy	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Paraplegia	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Spinal Cord Ischaemia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Transient Ischaemic Attack	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Psychiatric Disorders	3.4% (3/87)	0.0% (0/78)	0.0% (0/44)
Delirium Tremens	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Mental Status Changes	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Suicidal Ideation	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Renal and Urinary Disorders	1.1% (1/87)	2.6% (2/78)	2.3% (1/44)
Renal Failure Acute	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Ureteric Obstruction	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Urinary Bladder Polyp	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Urinary Incontinence	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Respiratory, Thoracic and Mediastinal Disorders	5.7% (5/87)	6.4% (5/78)	0.0% (0/44)
Acute Respiratory Failure	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Atelectasis	2.3% (2/87)	0.0% (0/78)	0.0% (0/44)
Chronic Obstructive Pulmonary Disease	1.1% (1/87)	3.8% (3/78)	0.0% (0/44)
Chylothorax	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Dyspnoea	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Hypoxia	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Pulmonary Congestion	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Pulmonary Embolism	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Respiratory Distress	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Vascular Disorders	8.0% (7/87)	6.4% (5/78)	6.8% (3/44)
Aortic Aneurysm	0.0% (0/87)	2.6% (2/78)	0.0% (0/44)
Aortic Dissection	2.3% (2/87)	0.0% (0/78)	0.0% (0/44)
Aortic Rupture	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)

Femoral Artery Occlusion	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Haemorrhage	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Hypertension	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Hypertensive Crisis	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Orthostatic Hypotension	0.0% (0/87)	1.3% (1/78)	2.3% (1/44)
Peripheral Artery Stenosis	0.0% (0/87)	0.0% (0/78)	2.3% (1/44)
Peripheral Artery Thrombosis	0.0% (0/87)	1.3% (1/78)	0.0% (0/44)
Peripheral Ischaemia	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)
Thrombophlebitis	1.1% (1/87)	0.0% (0/78)	0.0% (0/44)

[1]Number of subjects at risk at the beginning of the time interval and it is the denominator of event rate for the given time period.
[2]Percent (number) of subjects who experienced one or more serious AEs during the time period. A subject may report multiple adverse events and in different categories; hence, number of subjects in each category may not be the sum of those in each subcategory. Each subject was only counted once in each category.

Secondary Procedures

Table 36 displays the 3 secondary procedures that were performed through 365 days. All secondary procedures were adjudicated by the CEC to determine if the intervention performed was an MDE (a Valiant Evo Thoracic Stent Graft System related secondary procedure). Two secondary procedures were adjudicated as device-related (10309-002 and 11081-001), and one secondary procedure was not adjudicated as device-related (00341-001). The device-related secondary procedures both occurred within 30 days and included one secondary procedure (open surgery) in an attempt to treat a retrograde type A dissection and one secondary procedure (additional stent graft endovascular procedure) to treat an aortic arch rupture caused by septicemia following infection in a peripheral venous catheter. Both were counted against the primary endpoint. Please see the primary endpoint analysis above for more details. The one non-device related secondary procedure occurred at 70 days and included the repair of a left subclavian pseudoaneurysm and coil embolism of a Type II endoleak. There were no complications during the procedure and the subject had an uncomplicated post-operative course.

Table 36: Secondary Procedures within 365 Days

Subject #	Days from Implant	Type of Secondary Procedure: Reason (AE Term)
10309-002	1	Secondary Surgical Procedure: retrograde type A dissection
11081-001	28	Secondary Endovascular Procedure: aortic arch rupture due to septicemia

Subject #	Days from Implant	Type of Secondary Procedure: Reason (AE Term)
00341-001	70	Secondary Endovascular Procedure: Type II Endoleak

2. Additional Effectiveness Results

With regards to effectiveness, secondary endpoints were collected as shown in **Table 37**. The key effectiveness outcomes for this study are presented in **Table 38** through **Table 40**.

Table 37: Secondary Endpoints Based on Imaging Findings as Reported by Core Lab

Time Period Secondary Endpoints	Global Cohort
1 Month	
Loss of Stent Graft Patency at 1 Month	0.0% (0/81)
Endoleaks at 1 Month	2.5% (2/81)
6 Month	
Loss of Stent Graft Patency within 6 Months	0.0% (0/32)
Endoleaks at 6 Month	6.3% (2/32)
Stent Graft Migration at 6 Months	0.0% (0/36)
Aneurysm Expansion >5 mm at 6 Months	2.7% (1/37)
12 Month	
Loss of Stent Graft Patency within 12 Months	0.0% (0/21)
Endoleaks at 12 Month	9.5% (2/21)
Stent Graft Migration at 12 Months	0.0% (0/21)
Aneurysm Expansion >5 mm at 12 Months	9.5% (2/21)

Loss of Stent Graft Patency

At the time of the data snapshot, no loss of stent graft patency was reported by the core lab at any timepoint.

Endoleaks

All endoleaks, as reported by the core lab, are shown in **Table 38** below. A total of 2 endoleaks were reported globally at 1 month. A total of 2 endoleaks were reported globally at 6 months, one of which (Type Ia) was continuing from 1 month, and one of which was a new Type Ib endoleak. A total of 2 endoleaks were reported globally at 12 months, one of which (Type Ib) was continuing from 6 months, and one of which was a new Type Ib endoleak. The core lab did not review imaging performed during the procedure. The breakdown

of site-reported endoleaks by type in the global cohort is displayed in **Table 39** below.

Table 38: Endoleaks (All Subjects – Core Lab Reported)

Endoleaks	1 Month (1 – 90 Days)	6 Months (91 – 304 Days)	12 Months (305 – 548 Days)
Type I	1.2% (1/81)	6.3% (2/32)	9.5% (2/21)
Type Ia	1.2% (1/81)	3.1% (1/32)	0.0% (0/21)
Type Ib	0.0% (0/81)	3.1% (1/32)	9.5% (2/21)
Type Ic	0.0% (0/81)	0.0% (0/32)	0.0% (0/21)
Type II	1.2% (1/81)	0.0% (0/32)	0.0% (0/21)
Type III	0.0% (0/81)	0.0% (0/32)	0.0% (0/21)
Type IIIa	0.0% (0/81)	0.0% (0/32)	0.0% (0/21)
Type IIIb	0.0% (0/81)	0.0% (0/32)	0.0% (0/21)
Type IV	0.0% (0/81)	0.0% (0/32)	0.0% (0/21)
Type V	0.0% (0/81)	0.0% (0/32)	0.0% (0/21)
Type Undetermined	0.0% (0/81)	0.0% (0/32)	0.0% (0/21)
Subjects Had Endoleaks Of Any Type[1]	2.5% (2/81)	6.3% (2/32)	9.5% (2/21)

Note: Denominator is the number of subjects who had evaluable images in the time period.
[1]A subject may have more than one type of endoleaks; hence, number of subjects with any type may not be the sum of those in each type.

The breakdown of site-reported endoleaks by type in the global cohort is displayed in **Table 39**. Upon completion of the index procedure at day 0, a total of 5 (5.7%) endoleaks were reported by the sites, 1 Type Ib, 2 Type II, 1 Type IV, and 1 undetermined Type. At the 1-month follow-up visit, a total of 2 (2.5%) endoleaks were reported by the sites, both Type II endoleaks. At the 6-month follow-up visit, 2 (6.1%) Type II endoleaks were reported by the sites, 1 new and 1 continuing. At the 12-month follow-up visit, 1 (4.8%) new type 1b endoleak and 1 (4.8%) continuing Type II endoleak was reported.

Table 39: Endoleaks (All Subjects-Site Reported)

Endoleaks	Day 0	1 Month (1 – 90 Days)	6 Months (91 – 304 Days)	12 Months (305 – 548 Days)
Type I	1.1% (1/87)	0.0% (0/81)	0.0% (0/33)	4.8% (1/21)
Type Ia	0.0% (0/87)	0.0% (0/81)	0.0% (0/33)	0.0% (0/21)
Type Ib	1.1% (1/87)	0.0% (0/81)	0.0% (0/33)	4.8% (1/21)
Type Ic	0.0% (0/87)	0.0% (0/81)	0.0% (0/33)	0.0% (0/21)
Type II	2.3% (2/87)	2.5% (2/81)	6.1% (2/33)	4.8% (1/21)
Type III	0.0% (0/87)	0.0% (0/81)	0.0% (0/33)	0.0% (0/21)

Endoleaks	Day 0	1 Month (1 – 90 Days)	6 Months (91 – 304 Days)	12 Months (305 – 548 Days)
Type IIIa	0.0% (0/87)	0.0% (0/81)	0.0% (0/33)	0.0% (0/21)
Type IIIb	0.0% (0/87)	0.0% (0/81)	0.0% (0/33)	0.0% (0/21)
Type IV	1.1% (1/87)	0.0% (0/81)	0.0% (0/33)	0.0% (0/21)
Type V	0.0% (0/87)	0.0% (0/81)	0.0% (0/33)	0.0% (0/21)
Type Undetermined	1.1% (1/87)	0.0% (0/81)	0.0% (0/33)	0.0% (0/21)
Subjects Had Endoleaks Of Any Type[1]	4.6% (4/87)	2.5% (2/81)	6.1% (2/33)	9.5% (2/21)

Note: Denominator is the number of subjects who had evaluable images in the time period.

[1]A subject may have more than one type of endoleaks; hence, number of subjects with any type may not be the sum of those in each type.

Note: A type Ib endoleak was treated by secondary procedure on day 448 but was not reported in the site-reported images. This event was included in endoleaks event rate calculations.

Stent Graft Migration

At the time of the data snapshot, no stent graft migration was reported by the core lab at any timepoint.

Aneurysm Expansion

Table 40 below shows the change in aneurysm diameter and aneurysm expansion, as measured by the core lab.

At 6 months, a total of 1 subject (2.7%) (OUS) was reported to have a maximum aneurysm diameter that increased more than 5 mm at 6-months as compared to 1 month. The core lab indicated that for this subject the PAU did not increase in size, rather the increase in maximum aortic diameter is likely caused by expected dilatation of the aorta after TEVAR. No endoleaks were reported for this subject by the core lab nor the investigational site, and no interventions were performed associated with this reported expansion.

A total of 2 subjects (9.5%) (both OUS) were reported by the core lab to have a maximum aneurysm diameter increase of more than 5 mm between 1 month and 12 months. One of these subjects was the same subject that was reported to have a maximum aneurysm diameter increase at 6 months. No change in the aneurysm diameter between 6 and 12 months was reported for this subject. No endoleaks were reported for this subject and no inverventions were performed that were associated with this reported expansion. The other subject was reported to have a Type Ib endoleak due to distal aortic dilation resulting from aortic remodeling. A secondary procedure was performed on day 448 to resolve the Type Ib endoleak and distal aortic dilation.

Table 40: Change in Aneurysm Diameter (Core Lab)

Change in Maximum Aneurysm Diameter	Global Cohort
From 1 Month to 6 Months[1]	
Increase More Than 5 mm	2.7% (1/37)
Stable (within ± 5 mm)	83.8% (31/37)
Decrease More Than 5 mm	13.5% (5/37)
From 1 Month to 12 Months[1]	
Increase More Than 5 mm	9.5% (2/21)
Stable (within ± 5 mm)	66.7% (14/21)
Decrease More Than 5 mm	23.8% (5/21)

[1]Change in aneurysm diameter was compared to the 1-month contrast enhanced imaging measurement. When 1-month imaging was not available, the pre-discharge imaging was used as the baseline.

3. Subgroup Analyses
   The following preoperative characteristics were evaluated for potential association with outcomes: gender and race.

   There were no statistically significant differences by gender or race in the composite primary safety/effectiveness endpoint.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The Valiant Evo IDE study included 144 investigators (95 US and 49 OUS), none of whom were full-time or part-time employees of Medtronic. The types of compensation defined in 21 CFR 54.2 (a), (b), (c) and (f) are summarized below, along with the number of investigators reporting that type of compensation:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts (having a monetary value over $25,000): 4
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the panel, an FDA advisory committee, for review and recommendation because the information in the PMA-S substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM NONCLINICAL AND CLINICAL STUDIES

The Valiant Navion Thoracic Stent Graft System is the next generation Medtronic thoracic stent graft system. The Valiant Navion Thoracic Stent Graft System is expected to perform similarly to the Valiant Captivia Thoracic Stent Graft System, given the similarities between the materials, design and bench testing results of the two devices. The clinical study of the Valiant Navion Thoracic Stent Graft System was designed to evaluate the endpoints that were likely to be affected by the changes in the Valiant Navion Thoracic Stent Graft System as compared to the Valiant Captivia Thoracic Stent Graft System. The study of the Valiant Navion Thoracic Stent Graft System was limited to the evaluation of patients with aneursysms and penetrating ulcers based on clinical information available from studies of the Valiant Captivia Thoracic Stent Graft System which showed that treatment of aneurysms and penetrating ulcers represents an appropriate challenge to delivery and deployment.

Data regarding delivery and deployment of the Valiant Navion Thoracic Stent Graft System in the treatment of aneurysms and penetrating ulcers were extrapolated to apply to all isolated lesions of the descending thoracic aorta. The rationale for this approach is based on information from the studies of the Valiant Captivia Thoracic Stent Graft System.

A. Effectiveness Conclusions

The primary endpoint for the global cohort was a composite endpoint of safety and effectiveness. It was defined as the proportion of subjects with access failures,deployment failures, and/or MDEs within 30 days post index procedure. MDEs consisted of device-related secondary procedure, device related mortality, conversion to open surgery, or thoracic aneurysm rupture. Notably, the definition of deployment failures did not include deployment accuracy and did not consider the need for unplanned implantation of additional devices or the use of bailout procedures as deployment failures.

A pre-determined performance goal of 16% was established. The primary composite endpoint was met and was statistically significant, with a p-value of < 0.0001. A total of 2.3% (2/87) of subjects experienced the primary composite endpoint event within 30 days, with a 1-sided 97.5% upper confidence limit of 8.06%, lower than the performance goal of 16% (p-value <.0001). Two (2) subjects had a total of 4 MDEs within 30 days of the procedure; 1 subject had a device-related secondary procedure and device-related mortality and 1 subject had a thoracic aortic aneurysm rupture and device-related secondary procedure.

In addition to the primary endpoint outcome, additional observations were reported from the Valiant Evo IDE study which have been noted as device deficiencies. A total of 9.2% (8/87) of subjects were reported as having a device deficiency within 30 days, all occurring at the time of implant. Device deficienices reported in the study were as follows: failure to release tip capture, device distal movement and difficulty to remove delivery system. No device deficiencies were reported in any subject beyond 30 days. Four (4) of the reported deficiencies fit the more typical definition of delivery and deployment failure; 2 were associated with a failure in deployment accuracy with the need for placement of unplanned additional devices; and 2 resulted in the need for the use of bailout procedures.

An FDA requested post hoc analysis for the primary endpoint including the 4 additional events that would generally count against delivery and deployment success also met the primary composite endpoint. A total of 6.9% (6/87) subjects experienced the primary composite endpoint event within 30 days, with a 1-sided 97.5% upper confidence limit of 14.41%, lower than the performance goal of 16%.

The secondary endpoints evaluating the effectiveness of the Valiant Evo Thoracic Stent Graft System included evaluation of loss of stent graft patency and presence of endoleaks at 30 days, 6 months (applicable to US subjects only) and 12 months in the eligible subjects; additionally, migration and aneurysm expansion were evaluated at 6 months (applicable to US subjects only) and 12 months for the eligible subjects. No loss of stent graft patency was reported at any timepoint. Endoleaks were reported by core lab in two (2.5%) subjects at 1 month (one Type Ia and one Type II); at 6 months, two (6.3%) subjects reported endoleaks (continuing Type Ia and new Type Ib); and 12 months, a total of two (9.5%) subjects reported having an endoleak (both Type 1b, one new and one continuing). No stent graft migration, compared to the 1-month imaging, was reported at 6 months or 12 months. An aneurysm expansion of greater than 5 mm, compared to the 1-month imaging, was reported by the core lab in 1 subject (2.7%) at 6 months, and in 2 subjects (9.5%) at 12 months; the same subject that had the aneurysm expansion at 6 months was reported having this same observation at 12 months.

Based on the clinical endpoint outcomes presented above, there is reasonable assurance of effectiveness of the Valiant Navion Thoracic Stent Graft System for the proposed intended use.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory testing and animal studies, as well as data collected in a clinical study conducted to support PMA approval as described above.

As mentioned above, the primary composite endpoint of safety and effectiveness evaluation, access/deployment failures and MDEs within 30 days of the index procedure, was met for the global cohort. A total of 2.3% (2/87) of subjects experienced the primary composite endpoint event within 30 days which was significantly lower than the performance goal of 16%.

Secondary safety endpoints included major device effects, all-cause and aneurysm-related mortality, all adverse events (notably MAEs and SAEs), and secondary procedures at 0-30 days, 0-183 days and 0-365 days.

A total of six MDEs were reported within 365 days, of which 50% (3/6) were device-related mortalities, 33.3% (2/6) were device related secondary procedures, and 16.7% (1/6) was a thoracic aortic aneurysm (TAA) rupture.

With respect to mortality, between 0-365 days, a total of 6 subjects in the global cohort died, with two deaths between 0-30 days. One of the deaths was related to the device, procedure and aneurysm, and counted in the primary composite endpoint. Although the other death was aneurysm-related, it did not meet the definition of MDE, so was not counted in the primary composite endpoint. An additional three subjects died between 31-183 days, and one subject died between 184-365 days. A total of 3 out of the 6 deaths were adjudicated as aneurysm-related mortalities. Of the six deaths that occurred in the Valiant Evo US IDE study, three were device-related, and three were not device-related.

The following rates were reported for MAEs: 28.7% (25/87) from 0-30 days; 40.8% (31/76) from 0-183 days; and 45.3% (34/75) from 0-365 days. The following rates were reported for SAEs: 32.2% (28/87) from 0-30 days; 52.6% (40/76) from 0-183 days; and 9.7% (3/31) from 0-365 days.

There were 3 secondary procedures between 0-365 days; 1 to treat a retrograde Type A aortic dissection (1 day post index procedure), 1 to treat aortic arch rupture due to septicemia (28 days post index procedure), and one to treat a Type II endoleak (70 days post index procedure).

The reported event rates are not unexpected in this type of study.

Based on the study outcomes presented above, there is reasonable assurance of safety of the Valiant Navion Thoracic Stent Graft System for the proposed intended use.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA-S approval as described above. The Valiant Navion Thoracic Stent Graft System provides a broader range of device sizes and configurations, with controlled delivery of all configurations, and is delivered in smaller profile delivery systems as compared to the Valiant Captivia Thoracic Stent Graft System. These features offer the potential benefit to patients of reduced access complications. They may also expand the patient population that can be treated with a Medtronic thoracic stent graft.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA-S approval as described above. Notable procedure-related

AEs that were reported were a retrograde type A dissection (RTAD) and an aortic rupture; both events led to death of the subjects. Most MAEs and SAEs were related to periprocedural complications and the underlying comorbidities of study subjects. The types and rates of MAEs and SAEs are consistent with other studies of TEVAR for treatment of DTAA.

1. Patient Perspectives
   This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data supports that for the endovascular repair of lesions of the descending thoracic aorta the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The primary composite safety/effectiveness endpoint was met. The secondary enpoint outcomes are consistent with previous DTAA endovascular graft studies. Patients are likely to benefit from the use of this device to treat lesions of the descending thoracic aorta.

XIII. CDRH DECISION

CDRH issued an approval order on October 19, 2018. The final conditions of approval cited in the approval order are described below.

1. The sponsor agreed to include information regarding the Valiant Navion Thoracic Stent Graft System in the Valiant Annual Clinical Update, which they provide to physician users at least annually and include as part of the Valiant Annual Report per previous approval orders for this PMA. The information they have agreed to include regarding the Valiant Navion Thoracic Stent Graft System is as follows:
   a. Information from the Valiant EVO clinical study. At a minimum, this will include the number of patients for whom data are available and a summary of lesion-related deaths, aortic ruptures, aneurysm enlargements, major device effects, losses of device integrity, endoleaks, conversion to open surgical repair, and secondary interventions for these patients, including the reasons for the interventions.
   b. Relevant information from commercial experience of the Valiant Navion Thoracic Stent Graft System within and outside of the U.S.
   c. A summary of any explant analysis findings regarding the Valiant Navion Thoracic Stent Graft System.

   They have agreed to include this information in addition to the information required per the previous approval orders for this PMA.

2. Continued Follow-Up Valiant EVO Study: The Continued Follow-Up Valiant EVO Study is a prospective, non-randomized, multi-center, US and OUS, single arm, confirmatory study.

   The purpose of the Continued Follow-Up Valiant EVO Study is to obtain longer-term follow-up on the use of the Valiant Navion Thoracic Stent Graft System to treat descending thoracic aortic aneurysms. Five-year follow-up on the surviving patients from the 100 subjects enrolled in the IDE study, in accordance with the IDE protocol, will be reported. Clinical outcomes will include all-cause mortality, lesion-related mortality, major device effects, secondary procedures, conversion to open repair, occlusions and stenoses, endoleaks, stent graft migration, aneurysm expansion, aortic rupture, and losses of device integrity. These endpoints will be analyzed descriptively on a yearly basis.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See device labeling.

Hazards to Health from Use of Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post Approval Requirements and Restrictions: See approval order.